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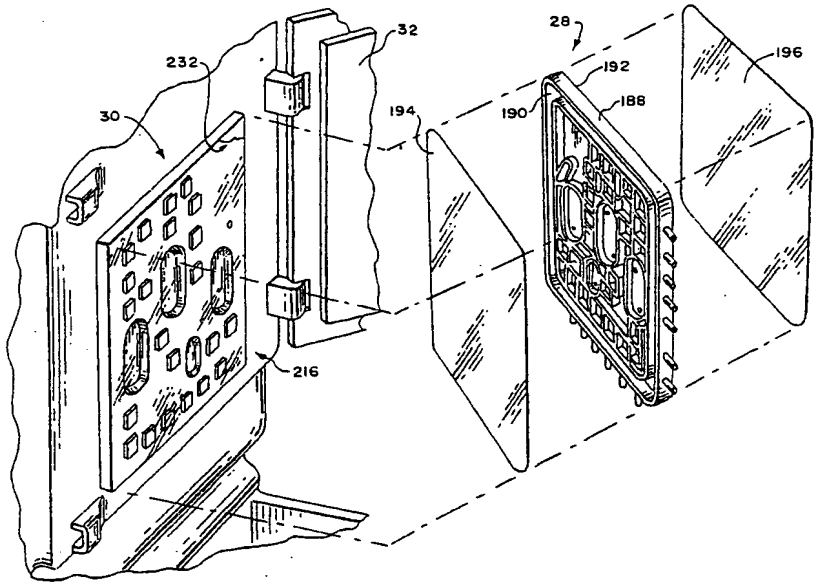
(54) Title: BLOOD SEPARATION SYSTEMS AND METHODS USING A MULTIPLE FUNCTION PUMP STATION TO PERFORM DIFFERENT ON-LINE PROCESSING TASKS



(57) Abstract: A multiple function pump station (PPN) performs different on-line processing tasks. The pump station can be operated in one mode to draw blood from a donor and can in another mode be operated to return blood to the donor. The pump station used to draw blood from a donor can also be used to perform subsequent blood processing tasks, such as mixing processing or additive fluids with the blood, or transferring a harvested blood component to a storage container, or finishing the processing of a harvested blood component, e.g., by passage through a filter (200) to remove leukocytes.

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cells, and platelets, can be realized in reasonable short processing times.

The operational and performance demands upon such fluid processing systems become more complex and sophisticated, even as the demand for smaller and more portable systems intensifies. The need therefore exists for automated blood processing controllers that can gather and generate more detailed information and control signals to aid the operator in maximizing processing and separation efficiencies.

Summary of the Invention

The invention provides systems and methods for processing blood and blood constituents that lend themselves to portable, flexible processing platforms equipped with straightforward and accurate control functions.

More particularly, the invention provides blood separation systems and methods, which employ a multiple function pump station to perform different on-line processing tasks. For example, a pump station that is operated in one mode to draw blood from a donor can, in another mode, be operated to return blood to the donor. As other examples, the pump station used to draw blood from a donor can also be used to perform subsequent blood processing tasks, such as mixing processing or additive fluids with the blood, or transferring a harvested blood component to a storage container, or finishing the processing of a harvested blood component, e.g., by passage through a filter to remove leukocytes.

The provision of a multiple function pump station makes consolidation of different processing tasks possible, and leads to a reduction in the overall size and complexity of a blood separation system. The use of a multiple function pump station also makes possible the performance of different blood processing procedures using the same blood separation system.

circulatory system of the donor, or by lowering the hematocrit of a returned cellular blood component, thereby allowing a larger gauge (i.e., smaller diameter) phlebotomy needle to be used.

In one embodiment, the pump station is operated in a processing fluid transfer mode, during which processing fluid in the utility flow channel into the blood processing flow channel for mixing with the blood component. In this arrangement, the processing fluid can includes a blood component additive to enhance storage of the blood component.

In one embodiment, the pump station includes a fluid pressure actuated pump and an actuator to apply fluid pressure to the pump. In this embodiment, the pump station and all the flow channels with which the pump station communicates are centralized within a cassette.

According to another aspect of the invention, a blood processing system and related method couple a pump station to a donor flow channel to convey fluid to and from a donor, a blood processing flow channel including a blood separation chamber to separate red blood cells from donor whole blood, and a blood component collection flow channel including a red blood cell collection container and an in-line filter to remove leukocytes from the red blood cells before entering the red blood cell collection container. The pump station is operated in a processing mode to convey whole blood in the donor flow channel into the blood processing flow channel for separation of the red blood cells in the blood separation chamber. The pump station is also operated in a collection mode, to convey at least some of the red blood cells in the blood processing flow channel into the blood component collection flow channel for on-line removal of leukocytes and collection in the red blood cell collection container.

In one embodiment applicable to each aspect of the

circuit, which can be programmed to perform a variety of different blood processing procedures in association with the device shown in Fig. 1;

Fig. 6 is an exploded perspective view of a cassette, which contains the programmable blood processing circuit shown in Fig. 5, and the pump and valve station on the processing device shown in Fig. 1, which receives the cassette for use;

Fig. 7 is a plane view of the front side of the cassette shown in Fig. 6;

Fig. 8 is an enlarged perspective view of a valve station on the cassette shown in Fig. 6;

Fig. 9 is a plane view of the back side of the cassette shown in Fig. 6;

Fig. 10 is a plane view of a universal processing set, which incorporates the cassette shown in Fig. 6, and which can be mounted on the device shown in Fig. 1, as shown in Figs. 2 and 3;

Fig. 11 is a top section view of the pump and valve station in which the cassette as shown in Fig. 6 is carried for use;

Fig. 12 is a schematic view of a pneumatic manifold assembly, which is part of the pump and valve station shown in Fig. 6, and which supplies positive and negative pneumatic pressures to convey fluid through the cassette shown in Figs. 7 and 9;

Fig. 13 is a perspective front view of the case that houses the processing device, with the lid open for use of the device, and showing the location of various processing elements housed within the case;

Fig. 14 is a schematic view of the controller that carries out the process control and monitoring functions of the device shown in Fig. 1;

Fig. 15A, 15B, and 15C are schematic side view of the blood separation chamber that the device shown in Fig.

the manner shown in Fig. 24, taken generally along line 24A-24A in Fig. 24;

Fig. 25 is a side section view of the molded processing container shown in Fig. 24, after connection of the umbilicus to container;

Fig. 26 is an exploded, perspective view of the centrifuge station of the processing device shown in Fig. 1, with the processing container mounted for use;

Fig. 27 is a further exploded, perspective view of the centrifuge station and processing container shown in Fig. 26;

Fig. 28 is a side section view of the centrifuge station of the processing device shown in Fig. 26, with the processing container mounted for use;

Fig. 29 is a top view of a molded centrifugal blood processing container as shown in Figs. 21 to 23, showing a flow path arrangement for separating whole blood into plasma and red blood cells;

Figs. 31 to 33 are top views of molded centrifugal blood processing containers as shown in Figs. 21 to 23, showing other flow path arrangements for separating whole blood into plasma and red blood cells;

Fig. 34 is a schematic view of another blood processing circuit, which can be programmed to perform a variety of different blood processing procedures in association with the device shown in Fig. 1;

Fig. 35 is plane view of the front side of a cassette, which contains the programmable blood processing circuit shown in Fig. 34;

Fig. 36 is a plane view of the back side of the cassette shown in Fig. 35;

Figs. 37A to 37E are schematic views of the blood processing circuit shown in Fig. 34, showing the programming of the cassette to carry out different fluid flow tasks in connection with processing whole blood into plasma and red

the features of the invention. The system 10 can be used for processing various fluids. The system 10 is particularly well suited for processing whole blood and other suspensions of biological cellular materials. Accordingly, the illustrated embodiment shows the system 10 used for this purpose.

I. System Overview

The system 10 includes three principal components. These are (i) a liquid and blood flow set 12; (ii) a blood processing device 14 that interacts with the flow set 12 to cause separation and collection of one or more blood components; and (iii) a controller 16 that governs the interaction to perform a blood processing and collection procedure selected by the operator.

The blood processing device 14 and controller 16 are intended to be durable items capable of long term use. In the illustrated and preferred embodiment, the blood processing device 14 and controller 16 are mounted inside a portable housing or case 36. The case 36 presents a compact footprint, suited for set up and operation upon a table top or other relatively small surface. The case 36 is also intended to be transported easily to a collection site.

The case 36 includes a base 38 and a hinged lid 40, which opens (as Fig. 1 shows) and closes (as Fig. 4 shows). The lid 40 includes a latch 42, for releasably locking the lid 40 closed. The lid 40 also includes a handle 44, which the operator can grasp for transporting the case 36 when the lid 40 is closed. In use, the base 38 is intended to rest in a generally horizontal support surface.

The case 36 can be formed into a desired configuration, e.g., by molding. The case 36 is preferably made from a lightweight, yet durable, plastic material.

The flow set 12 is intended to be a sterile, single use, disposable item. As Fig. 2 shows, before beginning a given blood processing and collection procedure, the

which will be described later.

Referring to Fig. 5, the circuit 46 can be programmed to perform a variety of different blood processing procedures in which, e.g., red blood cells are collected, or plasma is collected, or both plasma and red blood cells are collected, or the buffy coat is collected.

The circuit 46 includes several pump stations PP(N), which are interconnected by a pattern of fluid flow paths F(N) through an array of in line valves V(N). The circuit is coupled to the remainder of the blood processing set by ports P(N).

The circuit 46 includes a programmable network of flow paths, comprising eleven universal ports P1 to P8 and P11 to P13 and three universal pump stations PP1, PP2, and PP3. By selective operation of the in line valves V1 to V14, V16 to V18, and V21 to 23, any universal port P1 to P8 and P11 to P13 can be placed in flow communication with any universal pump station PP1, PP2, and PP3. By selective operation of the universal valves, fluid flow can be directed through any universal pump station in a forward direction or reverse direction between two valves, or an in-out direction through a single valve.

In the illustrated embodiment, the circuit also includes an isolated flow path comprising two ports P9 and P10 and one pump station PP4. The flow path is termed "isolated," because it cannot be placed into direct flow communication with any other flow path in the circuit 46 without exterior tubing. By selective operation of the in line valves V15, V19, and V20, fluid flow can be directed through the pump station in a forward direction or reverse direction between two valves, or an in-out direction through a single valve.

The circuit 46 can be programmed to assigned dedicated pumping functions to the various pump stations. For example, in a preferrred embodiment, the universal pump station PP3

blood processing procedure, to retain all or some of the buffy coat for storage, or to return all or some of the buffy coat to the donor.

In a preferred embodiment, the programmable fluid circuit 46 is implemented by use of a fluid pressure actuated cassette 28 (see Fig. 6). The cassette 28 provides a centralized, programmable, integrated platform for all the pumping and valving functions required for a given blood processing procedure. In the illustrated embodiment, the fluid pressure comprising positive and negative pneumatic pressure. Other types of fluid pressure can be used.

As Fig. 6 shows, the cassette 28 interacts with a pneumatic actuated pump and valve station 30, which is mounted in the lid of the 40 of the case 36 (see Fig. 1). The cassette 28 is, in use, mounted in the pump and valve station 30. The pump and valve station 30 apply positive and negative pneumatic pressure upon the cassette 28 to direct liquid flow through the circuit. Further details will be provided later.

The cassette 28 can take various forms. As illustrated (see Fig. 6), the cassette 28 comprises an injection molded body 188 having a front side 190 and a back side 192. For the purposes of description, the front side 190 is the side of the cassette 28 that, when the cassette 28 is mounted in the pump and valve station 30, faces away from the operator. Flexible diaphragms 194 and 196 overlay both the front side 190 and back sides 192 of the cassette 28, respectively.

The cassette body 188 is preferably made of a rigid medical grade plastic material. The diaphragms 194 and 196 are preferably made of flexible sheets of medical grade plastic. The diaphragms 194 and 196 are sealed about their peripheries to the peripheral edges of the front and back sides of the cassette body 188. Interior regions of the diaphragms 194 and 196 can also be sealed to interior regions of the cassette body 188.

is essentially flush with the surrounding surface of recessed valve well, and the valve seat 210 extends below than the surface of the valve well.

The flexible diaphragm 194 overlying the front side 190 of the cassette 28 rests against the upstanding peripheral edges surrounding the pump stations and valves. With the application of positive force uniformly against this side of the cassette body 188, the flexible diaphragm 194 seats against the upstanding edges. The positive force forms peripheral seals about the pump stations and valves. This, in turn, isolates the pumps and valves from each other and the rest of the system. The pump and valve station 30 applies positive force to the front side 190 of the cassette body 188 for this purpose.

Further localized application of positive and negative fluid pressures upon the regions of the diaphragm 194 overlying these peripherally sealed areas serve to flex the diaphragm regions in these peripherally sealed areas. These localized applications of positive and negative fluid pressures on these diaphragm regions overlying the pump stations serve to expel liquid out of the pump stations (with application of positive pressure) and draw liquid into the pump stations (with application of negative pressure).

In the illustrated embodiment, the bottom of each pump station PP1 to PP4 includes a recessed race 316 (see Fig. 7). The race 316 extends between the ports 202 and 204, and also includes a dogleg extending at an angle from the top port 202. The race 316 provides better liquid flow continuity between the ports 202 and 204, particularly when the diaphragm region is forced by positive pressure against the bottom of the pump station. The race 316 also prevents the diaphragm region from trapping air within the pump station. Air within the pump station is forced into the race 316, where it can be readily venting through the top port 202 out of the pump station, even if the diaphragm

on the back side 192 of the cassette 28.

The flexible diaphragms 194 and 196 overlying the front and back sides 190 and 192 of the cassette body 188 rest against the upstanding peripheral edges surrounding the liquid paths F1 to F38. With the application of positive force uniformly against the front and back sides 190 and 192 of the cassette body 188, the flexible diaphragms 194 and 196 seat against the upstanding edges. This forms peripheral seals along the liquid paths F1 to F38. In operation, the pump and valve station 30 applies positive force to the diaphragms 194 and 196 for this purpose.

The pre-molded ports P1 to P13 extend out along two side edges of the cassette body 188. The cassette 28 is vertically mounted for use in the pump and valve station 30(see Fig. 2). In this orientation, the ports P8 to P13 face downward, and the ports P1 to P7 are vertically stacked one above the other and face inward.

As Fig. 2 shows, the ports P8 to P13, by facing downward, are oriented with container support trays 212 formed in the base 38, as will be described later. The ports P1 to P7, facing inward, are oriented with the centrifuge station 20 and a container weigh station 214, as will also be described in greater detail later. The orientation of the ports P5 to P7 (which serve the processing chamber 18) below the ports P1 to P4 keeps air from entering the processing chamber 18.

This ordered orientation of the ports provides a centralized, compact unit aligned with the operative regions of the case 36.

B. The Universal Set

Fig. 10 schematically shows a universal set 264, which, by selective programming of the blood processing circuit 46 implemented by cassette 28, is capable of performing several different blood processing procedures.

The universal set 264 includes a donor tube 266, which

station, the umbilicus 296 links the rotating processing chamber 18 with the cassette 28 without need for rotating seals. Further details of this construction will be provided later.

The tubes 290, 292, and 294 are coupled, respectively, to the cassette ports P5, P6, and P7. The tube 290 conveys whole blood into the processing chamber 18. The tube 292 conveys plasma from the processing chamber 18. The tube 294 conveys red blood cells from processing chamber 18.

A plasma collection container 304 is coupled by a tube 302 to the cassette port P3. The collection container 304 is intended, in use, to serve as a reservoir for plasma during processing.

A red blood cell collection container 308 is coupled by a tube 306 to the cassette port P2. The collection container 308 is intended, in use, to receive a first unit of red blood cells for storage.

A whole blood reservoir 312 is coupled by a tube 310 to the cassette port P1. The collection container 312 is intended, in use, to serve as a reservoir for whole blood during processing. It can also serve to receive a second unit of red blood cells for storage.

As shown in Fig. 10, no tubing is coupled to the utility cassette port P13 and buffy port P4.

C. The Pump and Valve Station

The pump and valve station 30 includes a cassette holder 216. The door 32 is hinged to move with respect to the cassette holder 216 between the opened position, exposing the cassette holder 216 (shown in Fig. 6) and the closed position, covering the cassette holder 216 (shown in Fig. 3). The door 32 also includes an over center latch 218 with a latch handle 220. When the door 32 is closed, the latch 218 swings into engagement with the latch pin 222.

As Fig. 11 shows, the inside face of the door 32 carries an elastomeric gasket 224. The gasket 224 contacts

As Fig. 12 shows, the manifold 226 contains four pump actuators PA1 to PA4 and twenty-three valve actuators VA1 to VA23. The pump actuators PA1 to PA4 and the valve actuators VA1 to VA23 are mutually oriented to form a mirror image of the pump stations PP1 to PP4 and valve stations V1 to V23 on the front side 190 of the cassette 28.

As Fig. 22 also shows, each actuator PA1 to PA4 and VA1 to VA23 includes a port 228. The ports 228 convey positive or negative pneumatic pressures from the source in a sequence governed by the controller 16. These positive and negative pressure pulses flex the front diaphragm 194 to operate the pump chambers PP1 to PP4 and valve stations V1 to V23 in the cassette 28. This, in turn, moves blood and processing liquid through the cassette 28.

The cassette holder 216 preferably includes an integral elastomeric membrane 232 (see Fig. 6) stretched across the manifold assembly 226. The membrane 232 serves as the interface between the piston element 226 and the diaphragm 194 of the cassette 28, when fitted into the holder 216. The membrane 232 may include one or more small through holes (not shown) in the regions overlying the pump and valve actuators PA1 to PA4 and V1 to V23. The holes are sized to convey pneumatic fluid pressure from the manifold assembly 226 to the cassette diaphragm 194. Still, the holes are small enough to retard the passage of liquid. The membrane 232 forms a flexible splash guard across the exposed face of the manifold assembly 226.

The splash guard membrane 232 keeps liquid out of the pump and valve actuators PA1 to PA4 and VA1 to VA23, should the cassette diaphragm 194 leak. The splash guard membrane 232 also serves as a filter to keep particulate matter out of the pump and valve actuators of the manifold assembly 226. The splash guard membrane 232 can be periodically wiped clean when cassettes 28 are exchanged.

The manifold assembly 226 includes an array of solenoid

valves V1 to V23. Pinpr is applied to drive the expression of liquid from the in-process pump PP1 and the plasma pump PP2. A typical pressure level for Phard and Pinpr in the context of the preferred embodiment is 500 mmHg.

(ii) Pgen, or General Pressure, is applied to drive the expression of liquid from the donor interface pump PP3 and the anticoagulant pump PP4. A typical pressure level for Pgen in the context of the preferred embodiment is 150 mmHg.

(iii) Pcuff, or Cuff Pressure, is supplied to the donor pressure cuff. A typical pressure level for Pcuff in the context of the preferred embodiment is 80 mmHg.

(iv) Vhard, or Hard Vacuum, is the deepest vacuum applied in the manifold assembly 226. Vhard is applied to open cassette valves V1 to V23. A typical vacuum level for Vhard in the context of the preferred embodiment is -350 mmHg.

(vi) Vgen, or General Vacuum, is applied to drive the draw function of each of the four pumps PP1 to PP4. A typical pressure level for Vgen in the context of the preferred embodiment is -300 mmHg.

(vii) Pdoor, or Door Pressure, is applied to the bladder 314 to seal the cassette 28 into the holder 216. A typical pressure level for Pdoor in the context of the preferred embodiment is 700 mmHg.

For each pressure and vacuum level, a variation of plus or minus 20 mmHg is tolerated.

Pinpr is used to operate the in process pump PP1, to pump blood into the processing chamber 18. The magnitude of Pinpr must be sufficient to overcome a minimum pressure of approximately 300 mm Hg, which is typically present within the processing chamber 18.

Similarly, Pinpr is used for the plasma pump PP2, since it must have similar pressure capabilities in the event that plasma needs to be pumped backwards into the processing chamber 18, e.g., during a spill condition, as will be

326 monitors Pgen. The sensor 32 controls a solenoid 30. The solenoid 30 is normally closed. The sensor S2 opens the solenoid 30 to refresh Pgen from the hard pressure line 322, up to the maximum value of Pgen. Solenoid 30 is closed as long as Pgen is within its specified pressure range and is opened when Pgen falls outside its specified range.

An in process pressure line 328 also branches from the hard pressure line 322. A sensor S3 in the in process pressure line 328 monitors Pinpr. The sensor S3 controls a solenoid 36. The solenoid 36 is normally closed. The sensor S3 opens the solenoid 36 to refresh Pinpr from the hard pressure line 322, up to the maximum value of Pinpr. Solenoid 36 is closed as long as Pinpr is within its specified pressure range and is opened when Pinpr falls outside its specified range.

A general vacuum line 330 branches from the hard vacuum line 324. A sensor S6 monitors Vgen in the general vacuum line 330. The sensor S6 controls a solenoid 31. The solenoid 31 is normally closed. The sensor S6 opens the solenoid 31 to refresh Vgen from the hard vacuum line 324, up to the maximum value of Vgen. The solenoid 31 is closed as long as Vgen is within its specified range and is opened when Vgen falls outside its specified range.

In-line reservoirs R1 to R5 are provided in the hard pressure line 322, the in process pressure line 328, the general pressure line 326, the hard vacuum line324, and the general vacuum line 330. The reservoirs R1 to R5 assure that the constant pressure and vacuum adjustments as above described are smooth and predictable.

The solenoids 33 and 34 provide a vent for the pressures and vacuums, respectively, upon procedure completion. Since pumping and valving will continually consume pressure and vacuum, the solenoids 33 and 34 are normally closed. The solenoids 33 and 34 are opened to vent the manifold assembly upon the completion of a blood

donor will relax (vent) the solenoid 42 to close the occluder 320 and isolate the donor. Similarly, any loss of power will relax the solenoid 42 and isolate the donor.

The sensor S4 monitors Pcuff and communicates with solenoids 41 (for increases in pressure) and solenoid 40 (for venting) to maintain the donor cuff within its specified ranges during the procedure. The solenoid 40 is normally open so that the cuff line will vent in the event of system error or loss of power. The solenoid 41 is normally closed to isolate the donor from any Phard in the event of power loss or system error.

Fig. 12 shows a sensor S8 in the pneumatic line serving the donor interface pump actuator PA3. The sensor S8 is a bi-directional mass air flow sensor, which can monitor air flow to the donor interface pump actuator PA3 to detect occlusions in the donor line. Alternatively, as will be described in greater detail later, electrical field variations can be sensed by an electrode carried within the donor interface pump chamber PP3, or any or all other pump chambers PP1, PP2, or PP4, to detect occlusions, as well as to permit calculation of flow rates and the detection of air.

Various alternative embodiments are possible. For example, the pressure and vacuum available to the four pumping chambers could be modified to include more or less distinct levels or different groupings of "shared" pressure and vacuum levels. As another example, Vhard could be removed from access to the solenoids 2, 5, 8, 18, 19, 21, 22 since the restoring springs will return the cassette valves to a closed position upon removal of a vacuum. Furthermore, the vents shown as grouped together could be isolated or joined in numerous combinations.

It should also be appreciated that any of the solenoids used in "normally open" mode could be re-routed pneumatically to be realized as "normally closed".

controller to control processing events will be provided later.

The holding trays 212 comprise molded recesses in the base 38. The trays 212 accommodate the containers 276 and 280 (see Fig. 2). In the illustrated embodiment, an additional swing-out hanger 248 is also provided on the side of the lid 40. The hanger 248 (see Fig. 2) supports the container 288 during processing. In the illustrated embodiment, the trays 212 and hanger 248 also include weigh sensors 246.

The weigh sensors 246 can be variously constructed. In the embodiment shown in Fig. 40, the scale includes a force sensor 404 incorporated into a housing 400, to which a hanger 402 is attached. The top surface 420 of hanger 402 engages a spring 406 on the sensor 404. Another spring 418 is compressed as a load, carried by the hanger 402, is applied. The spring 418 resists load movement of the hanger 402, until the load exceeds a predetermined weight (e.g., 2 kg.). At that time, the hanger 402 bottoms out on mechanical stops 408 in the housing 400, thereby providing over load protection.

In the embodiment shown in Fig. 41, a supported beam 410 transfers force applied by a hanger 416 to a force sensor 412 through a spring 414. This design virtually eliminates friction from the weight sensing system. The magnitude of the load carried by the beam is linear in behavior, and the weight sensing system can be readily calibrated to ascertain an actual load applied to the hanger 416.

B. The Controller and Operator Interface Station

The controller 16 carries out process control and monitoring functions for the system 10. As Fig. 14 shows schematically, the controller 16 comprises a main processing unit (MPU) 250, which can comprise, e.g., a Pentium™ type microprocessor made by Intel Corporation, although other

illustrated embodiment shows five units 256(1) to 256 (5). The slave processing units 256 (1) to 256 (5), in turn, communicates with low level peripheral controllers 258 for controlling the pneumatic pressures within the manifold assembly 226, the weigh sensors 246, the pump and valve actuators PA1 to PA4 and VA1 to VA23 in the pump and valve station 30, the motor for the centrifuge station 20, the interface sensing station 332, and other functional hardware of the system.

The MPU 250 contains in EPROM's the commands for the peripheral controllers 258, which are downloaded to the appropriate slave processing unit 256(1) to 256(5) at start-up. The application control manager 252 also downloads to the appropriate slave processing unit 256(1) to 256(5) the operating parameters prescribed by the activated application 254.

With this downloaded information, the slave processing units 256(1) to 256(5) proceed to generate device commands for the peripheral controllers 258, causing the hardware to operate in a specified way to carry out the procedure. The peripheral controllers 258 return current hardware status information to the appropriate slave processing unit 256(1) to 256(5), which, in turn, generate the commands necessary to maintain the operating parameters ordered by the application control manager 252.

In the illustrated embodiment, one slave processing unit 256(2) performs the function of an environmental manager. The unit 256(2) receives redundant current hardware status information and reports to the MPU 250 should a slave unit malfunction and fail to maintain the desired operating conditions.

As Fig. 14 shows, the MPU 250 also includes an interactive user interface 260, which allows the operator to view and comprehend information regarding the operation of the system 10. The interface 260 is coupled to the

T_{Pump} is the time the fluid is moved out of the pump chamber.

T_{Fill} is the time the pump is filled with fluid, and

T_{Idle} is the time when the pump is idle, that is, when no fluid movement occurs.

The SV can be affected by the interaction of the pump with attached downstream and upstream fluid circuits. This is analogous, in electrical circuit theory, to the interaction of a non-ideal current source with the input impedance of the load it sees. Because of this, the actual SV can be different than the nominal SV.

The actual fluid flow in volume per unit of time Q_{Actual} can therefore be expressed as follows:

$$Q_{Actual} = k \times \frac{SV_{Ideal}}{T_{Pump} + T_{Fill} + T_{Idle}} \quad (2)$$

where:

Q_{Actual} is the actual fluid flow in volume per unit of time.

SV_{Ideal} is the theoretical stroke volume, based upon the geometry of the pump chamber. k is a correction factor that accounts for the interactions between the pump and the upstream and downstream pressures.

The actual flow rate can be ascertained gravimetrically, using the upstream or downstream weigh scales 246, based upon the following relationship:

$$Q_{Actual} = \frac{\Delta Wt}{\rho \times \Delta T} \quad (3)$$

where:

ΔWt is the change in weight of fluid as detected by the upstream or downstream weigh scale 246 during the time period ΔT,

ρ is the density of fluid.

ΔT is the time period where the change in weight ΔWt is detected in the weigh scale 246.

The following expression is derived by combining

With the weigh scales 246, the controller 16 can perform on-line diagnostics even if the pumps are not moving fluid. For example, if the weigh scales 246 detect changes in weight when no flow is expected, then a leaky valve or a leak in the set 264 may be present.

In computing k and T_{idle} and/or T_{Pump} and/or T_{Fill}, the controller 16 may rely upon multiple measurements of ΔWt and/or ΔT. A variety of averaging or recursive techniques (e.g., recursive least means squares, Kalman filtering, etc.) may be used to decrease the error associated with the estimation schemes.

The above described monitoring technique is applicable for use for other constant stroke volume pumps, i.e. peristaltic pumps, etc.

2. Electrical Monitoring

In an alternative arrangement (see Fig. 42), the controller 16 includes a metal electrode 422 located in the chamber of each pump station PP1 to PP4 on the cassette 28. The electrodes 422 are coupled to a current source 424. The passage of current through each electrode 422 creates an electrical field within the respective pump chamber PP1 to PP4.

Cyclic deflection of the diaphragm 194 to draw fluid into and expel fluid from the pump chamber PP1 to PP4 changes the electrical field, resulting in a change in total capacitance of the circuit through the electrode 422. Capacitance increases as fluid is draw into the pump chamber PP1 to PP4, and capacitance decreases as fluid is expelled from pump chamber PP1 to PP4.

The controller 16 includes a capacitive sensor 426 (e.g., a Qprox E2S)coupled to each electrode 422. The capacitive sensor 426 registers changes in capacitance for the electrode 422 in each pump chamber PP1 to PP4. The capacitance signal for a given electrode 422 has a high signal magnitude when the pump chamber is filled with liquid

A. Double RBC Collection Procedure (No Plasma Collection)

During this procedure, whole blood from a donor is centrifugally processed to yield up to two units (approximately 500 ml) of red blood cells for collection. All plasma constituent is returned to the donor. This procedure will, in shorthand, be called the double red blood cell collection procedure.

Prior to undertaking the double red blood cell collection procedure, as well as any blood collection procedure, the controller 16 operates the manifold assembly 226 to conduct an appropriate integrity check of the cassette 28, to determine whether there are any leaks in the cassette 28. Once the cassette integrity check is complete and no leaks are found, the controller 16 begins the desired blood collection procedure.

The double red blood cell collection procedure includes a pre-collection cycle, a collection cycle, a post-collection cycle, and a storage preparation cycle. During the pre-collection cycle, the set 264 is primed to vent air prior to venipuncture. During the collection cycle, whole blood drawn from the donor is processed to collect two units of red blood cells, while returning plasma to the donor. During the post-collection cycle, excess plasma is returned to the donor, and the set is flushed with saline. During the storage preparation cycle, a red blood cell storage solution is added.

1. The Pre-Collection Cycle

a. Anticoagulant Prime

In a first phase of the pre-collection cycle (AC Prime 1), tube 300 leading to the phlebotomy needle 268 is clamped closed (see Fig. 10). The blood processing circuit 46 is programmed (through the selective application of pressure to the valves and pump stations of the cassette) to operate the donor interface pump PP3, drawing anticoagulant through the

(Saline Prime 2). The processing chamber 46 is rotated at a low rate (e.g., about 300 RPM), while the circuit continues to operate in the same fashion as in Saline Prime 3. Additional saline is drawn into the pump station PP1 through valve V14 and expelled out of the pump station PP1 through valve V9 and into the in-process container 312. Weight changes in the in-process container 312 are monitored. This phase is terminated upon registering a predetermined weight change in the in-process container 312, which indicates the conveyance of an additional volume of saline sufficient to substantially fill the processing chamber 46 (e.g., about 80 g).

In a fifth phase of the pre-collection cycle (Saline Prime 3), the circuit is programmed to first operate the in-process pump station PP1 to convey saline from the in-process container 312 through all outlet ports of the separation device and back into the saline container 288 through the plasma pump station PP2. This completes the priming of the processing chamber 46 and the in-process pump station PP1 (pumping in through valve V9 and out through valve V14), as well as primes the plasma pump station PP2, with the valves V7, V6, V10, and V12 opened to allow passive flow of saline. During this time, the rate at which the processing chamber 46 is rotated is successively ramped between zero and 300 RPM. Weight changes in the in process container 312 are monitored. When a predetermined initial volume of saline is conveyed in this manner, the circuit is programmed to close valve V7, open valves V9 and V14, and to commence pumping saline to the saline container 288 through the plasma pump PP2, in through valve V12 and out through valve V10, allowing saline to passively flow through the in-process pump PP1. Saline in returned in this manner from the in-process container 312 to the saline container 288 until weight sensing indicated that a preestablished minimum volume of saline occupies the in-process container 312.

TABLE

Programming of Blood Processing Circuit During Pre-Collection Cycle

(Double Red Blood Cell Collection Procedure)

Phase	AC Prime 1	AC Prime 2	Saline Prime 1	Saline Prime 2	Saline Prime 3	Vent Donor Line	Veni-puncture
V1	•	•	•	•	•	•	•
V2	•	•	•	•	•	•	•
V3	o	o	•	•	•	o	•
V4	•	•	o	•	•	•	•
V5	•	•	•	•	•	•	•
V6	•	•	•	•	o	•	•
V7	•	•	•	•	o	•	•
V8	•	•	•	•	•	•	•
V9	•	•	o/• Pump Out	o/• Pump Out	o/• Pump In (Stage 1) o (Stage 2)	•	•
V10	•	•	•	•	o (Stage 1) o/• Pump Out (Stage 2)	•	•
V11	o/• Pump Out	o	•	•	•	o/• Pump In	•
V12	•	•	•	•	o (Stage 1) o/• Pump In (Stage 2)	•	•
V13	o/• Pump In	o	•	•	•	o/• Pump Out	•

cycle (Blood Prime 1), the blood processing circuit 46 is programmed (through the selective application of pressure to the valves and pump stations of the cassette) to operate the donor interface pump PP3 (i.e., in through valve V13 and out through valve V11) and the anticoagulant pump PP4 (i.e., in through valve V20 and out through valve V15) to draw anticoagulated blood through the donor tube 270 into the in process container 312. This phase continues until an incremental volume of anticoagulated whole blood enters the in process container 312, as monitored by the weigh sensor.

In a next phase (Blood Prime 2), the blood processing circuit 46 is programmed to operate the in-process pump station PP1 to draw anticoagulated blood from the in-process container 312 through the separation device. During this phase, saline displaced by the blood is returned to the donor. This phase primes the separation device with anticoagulated whole blood. This phase continues until an incremental volume of anticoagulated whole blood leaves the in process container 312, as monitored by the weigh sensor.

B. Blood Separation While Drawing Whole Blood or Without Drawing Whole Blood

In a next phase of the blood collection cycle (Blood Separation While Drawing Whole Blood), the blood processing circuit 46 is programmed to operate the donor interface pump station PP3 (i.e., in through valve V13 and out through valve V11); the anticoagulant pump PP4 (i.e., in through valve V20 and out through valve V15); the in-process pump PP1 (i.e., in through valve V9 and out through valve V14); and the plasma pump PP2 (i.e., in through valve V12 and out through valve V10). This arrangement draws anticoagulated blood into the in-process container 312, while conveying the blood from the in-process container 312 into the processing chamber for separation. This arrangement also removes plasma from the processing chamber into the plasma container 304, while removing red blood cells from the processing chamber

V9 and out through valve V14); and the plasma pump PP2 (i.e., in through valve V12 and out through valve V10). This arrangement conveys anticoagulated whole blood from the in-process container 312 into the processing chamber for separation, while removing plasma into the plasma container 304 and red blood cells into the red blood cell container 308. This arrangement also conveys plasma from the plasma container 304 to the donor, while also mixing saline from the container 288 in line with the returned plasma. The in line mixing of saline with plasma raises the saline temperature and improves donor comfort. This phase continues until the plasma container 304 is empty, as monitored by the weigh sensor.

If the volume of whole blood in the in-process container 312 reaches a specified low threshold before the plasma container 304 empties, the circuit is programmed to enter another phase (Return Plasma Without Separation), to terminate operation of the in-process pump station PP1 (while also closing valves V9, V10, V12, and V14) to terminate blood separation. The phase continues until the plasma container 304 empties.

Upon emptying the plasma container 304, the circuit is programmed to enter a phase (Fill Donor Line), to operate the donor interface pump station PP3 (i.e., in through valve V11 and out through valve V13) to draw whole blood from the in process container 312 to fill the donor tube 266, thereby purge plasma (mixed with saline) in preparation for another draw whole blood cycle.

The circuit is then programmed to conduct another Blood Separation While Drawing Whole Blood Phase, to refill the in process container 312. The circuit is programmed in successive Blood Separation and Return Plasma Phases until the weigh sensor indicates that a desired volume of red blood cells have been collected in the red blood cell collection container 308. When the targeted volume of red

Phase	Blood Prime 1	Blood Prime 2	Blood Separation While Drawing Whole Blood (Without Drawing Whole Blood)	Return Plasma/ with Separation (Without Separation)	Fill Donor Line
V14	●	o/● Pump Out	o/● Pump Out	o/● Pump Out (●)	●
V15	o/● Pump Out	●	o/● Pump Out (●)	●	●
V16	●	●	●	●	●
V17	●	●	●	●	●
V18	o	o	o (●)	o	o
V19	o	●	o (●)	●	●
V20	o/● Pump Out	●	o/● Pump In (●)	●	●
V21	●	●	●	●	●
V22	●	●	●	o	●
V23	●	●	●	o/● Alternates with V6	●
PP1	■	□	□	□ (■)	■
PP2	■	■	□	□ (■)	■
PP3	□	■	□ (■)	□	□
PP4	□	■	□ (■)	■	■

Caption: o denotes an open valve; ● denotes a closed valve; o/● denotes a valve opening and closing during a pumping sequence; ■ denotes an idle pump station (not in use); and □ denotes a pump station in use.

D. **The Post-Collection Cycle**

Once the targeted volume of red blood cells has been

In the next phase (Fluid Replacement), the circuit is programmed to operate the donor interface pump station PP3 (i.e., in through valve V11 and out through valve V13) to convey the saline to the donor. This phase continues until a prescribed replacement volume amount is infused, as monitored by the weigh sensor.

In the next phase of the post-collection cycle (Empty In Process Container), the circuit is programmed to operate the donor interface pump station PP3 (i.e., in through valve V11 and out through valve V13) to convey all remaining contents of the in-process container 312 to the donor, in preparation of splitting the contents of the red blood cell container 308 for storage in both containers 308 and 312. This phase continues until a zero volume reading for the in-process container 312 occurs, as monitored by the weigh sensor, and air is detected at the air detector.

At this phase, the circuit is programmed to close all valves and idle all pump stations, so that the phlebotomy needle 268 can be removed from the donor.

The programming of the circuit during the phases of the post-collection cycle is summarized in the following table.

TABLE

Programming of Blood Processing Circuit During The Post-Collection Cycle

(Double Red Blood Cell Collection Procedure)

Phase	Excess Plasma Return	Saline Purge	Final Return	Fluid Replacement	Empty In Process Container
V1	•	•	o	•	o
V2	•	•	•	•	•
V3	•	•	•	•	•
V4	•	o	•	•	•
V5	o	•	•	•	•
V6	o/• Alternates with V23	•	•	•	•

o/• denotes a valve opening and closing during a pumping sequence; ■ denotes an idle pump station (not in use); and □ denotes a pump station in use.

E. The Storage Preparation Cycle

1. Split RBC

In the first phase of the storage preparation cycle (Split RBC), the circuit is programmed to operate the donor interface pump station PP3 to transfer half of the contents of the red blood cell collection container 308 into the in-process container 312. The volume pumped is monitored by the weigh sensors for the containers 308 and 312.

2. Add RBC Preservative

In the next phases of the storage preparation cycle (Add Storage Solution to the In Process Container and Add Storage Solution to the Red Blood Cell Collection Container), the circuit is programmed to operate the donor interface pump station PP3 to transfer a desired volume of red blood cell storage solution from the container 280 first into the in-process container 312 and then into the red blood cell collection container 308. The transfer of the desired volume is monitored by the weigh scale.

In the next and final phase (End Procedure), the circuit is programmed to close all valves and idle all pump stations, so that the red blood cell containers 308 and 312 can be separated and removed for storage. The remainder of the disposable set can now be removed and discarded.

The programming of the circuit during the phases of the storage preparation cycle is summarized in the following table.

TABLE

Programming of Blood Processing Circuit During The Storage Preparation Cycle

(Double Red Blood Cell Collection Procedure)

Phase	Split RBC Between RBC Collection and In Process Containers	Add Storage Solution to In Process Container	Add Storage Solution to RBC Collection Container	End Procedure (Remove Veni-puncture)
PP2	■	■	■	■
PP3	□	□	□	■
PP4	■	■	■	■

Caption: o denotes an open valve; • denotes a closed valve; o/• denotes a valve opening and closing during a pumping sequence; ■ denotes an idle pump station (not in use); and □ denotes a pump station in use.

F. Plasma Collection (No Red Blood Cell Collection)

During this procedure, whole blood from a donor is centrifugally processed to yield up to 880 ml of plasma for collection. All red blood cells are returned to the donor. This procedure will, in shorthand, be called the plasma collection procedure.

Programming of the blood processing circuit 46 (through the selective application of pressure to the valves and pump stations of the cassette) makes it possible to use the same universal set 264 as in the double red blood cell collection procedure.

The procedure includes a pre-collection cycle, a collection cycle, and a post-collection cycle.

During the pre-collection cycle, the set 264 is primed to vent air prior to venipuncture. During the collection cycle, whole blood drawn from the donor is processed to collect plasma, while returning red blood cells to the donor. During the post-collection cycle, excess plasma is returned to the donor, and the set is flushed with saline.

1. The Pre-Collection Cycle

a. Anticoagulant Prime

In the pre-collection cycle for the plasma collection (no red blood cells) procedure, the cassette is programmed

Phase	AC Prime 1	AC Prime 2	Saline Prime 1	Saline Prime 2	Saline Prime 3	Vent Donor Line	Veni-puncture
V10	•	•	•	•	o (Stage 1) o/• Pump Out (Stage 2)	•	•
V11	o/• Pump Out	o	•	•	•	o/• Pump In	•
V12	•	•	•	•	o (Stage 1) o/• Pump In (Stage 2)	•	•
V13	o/• Pump In	o	•	•	•	o/• Pump Out	•
V14	•	•	o/• Pump In	o/• Pump In	o/• Pump Out (Stage 1) o (Stage 2)	•	•
V15	o	o/• Pump In Pump Out	•	•	•	o	•
V16	•	•	•	•	•	•	•
V17	•	•	•	•	•	•	•
V18	o	o	•	•	•	o	•
V19	o	o	•	•	•	o	•
V20	o	o/• Pump Out Pump In	•	•	•	o	•
V21	•	•	•	•	•	•	•
V22	•	•	o	o	o	•	•
V23	•	•	o	o	o	•	•

Whole Blood or Without Drawing Whole Blood

In a next phase of the blood collection cycle (Blood Separation While Drawing Whole Blood), the blood processing circuit 46 is programmed to operate the donor interface pump station PP3 (i.e., in through valve V13 and out through valve V11); the anticoagulant pump PP4 (i.e., in through valve V20 and out through valve V15); the in-process pump PP1 (i.e., in through valve V9 and out through valve V14); and the plasma pump PP2 (i.e., in through valve V12 and out through valve V10), in the same fashion as the Blood Separation While Drawing Whole Blood Phase for the double red blood cell collection procedure, as already described. This arrangement draws anticoagulated blood into the in-process container 312, while conveying the blood from the in-process container 312 into the processing chamber for separation. This arrangement also removes plasma from the processing chamber into the plasma container 304, while removing red blood cells from the processing chamber into the red blood cell container 308. This phase continues until the targeted volume of plasma is collected in the plasma collection container 304 (as monitored by the weigh sensor) or until a targeted volume of red blood cells is collected in the red blood cell collection container (as monitored by the weigh sensor).

As in the double red blood cell collection procedure, if the volume of whole blood in the in-process container 312 reaches a predetermined maximum threshold before the targeted volume of either plasma or red blood cells is collected, the circuit is programmed to enter another phase (Blood Separation Without Drawing Whole Blood), to terminate operation of the donor interface pump station PP3 (while also closing valves V13, V11, V18, and V13) to terminate collection of whole blood in the in-process container 312, while still continuing blood separation. If the volume of

the red blood cell container 308 is empty, as monitored by the weigh sensor.

If the volume of whole blood in the in-process container 312 reaches a specified low threshold before the red blood cell container 308 empties, the circuit is programmed to enter another phase (Red Blood Cell Return Without Separation), to terminate operation of the in-process pump station PP1 (while also closing valves V9, V10, V12, and V14) to terminate blood separation. The phase continues until the red blood cell container 308 empties.

Upon emptying the red blood cell container 308, the circuit is programmed to enter another phase (Fill Donor Line), to operate the donor interface pump station PP3 (i.e., in through valve V11 and out through valve V13) to draw whole blood from the in process container 312 to fill the donor tube 266, thereby purge red blood cells (mixed with saline) in preparation for another draw whole blood cycle.

The circuit is then programmed to conduct another Blood Separation While Drawing Whole Blood Phase, to refill the in process container 312. The circuit is programmed to conduct successive draw whole blood and return red blood cells / saline cycles, as dsecribed, until the weigh sensor indicates that a desired volume of plasma has been collected in the plasma collection container 304. When the targeted volume of plasma has been collected, the post-collection cycle commences.

The programming of the circuit during the phases of the collection cycle is summarized in the following table.

TABLE

Programming of Blood Processing Circuit During The Collection Cycle

(Plasma Collection Procedure)

Phase	Blood Prime 1	Blood Prime 2	Blood Separation While Drawing Whole Blood (Without Drawing Whole Blood)	Return Red Blood Cells / Saline with Separation (Without Separation)	Fill Donor Line
V19	o	•	o (•)	•	•
V20	o/• Pump Out	•	o/• Pump In (•)	•	•
V21	•	•	•	•	•
V22	•	•	•	o	•
V23	•	•	•	o/• Alternates with V7	•
PP1	■	□	□	□ (■)	■
PP2	■	■	□	□ (■)	■
PP3	□	■	□ (■)	□	□
PP4	□	■	□ (■)	■	■

Caption: o denotes an open valve; • denotes a closed valve; o/• denotes a valve opening and closing during a pumping sequence; ■ denotes an idle pump station (not in use); and □ denotes a pump station in use.

d. The Post-Collection Cycle

Once the targeted volume of plasma has been collected (as monitored by the weigh sensor), the circuit is programmed to carry out the phases of the post-collection cycle.

3. Return Excess Red Blood Cells

In a first phase of the post-collection cycle (Remove Plasma Collection Container), the circuit is programmed to close all valves and disable all pump stations to allow separation of the plasma collection container 304 from the

convey the saline to the donor. This phase continues until a prescribed replacement volume amount is infused, as monitored by the weigh sensor.

In the final phase (End Procedure), the circuit is programmed to close all valves and idle all pump stations, so that venipuncture can be terminated, and the plasma container can be separated and removed for storage. The remaining parts of the disposable set can be removed and discarded.

The programming of the circuit during the phases of the post-collection cycle is summarized in the following table.

TABLE

Programming of Blood Processing Circuit During The Post-Collection Cycle

(Plasma Collection Procedure)

Phase	Remove Plasma Collection Container	Return RBC	Saline Purge	Final Return	Fluid Replacement	End Procedure
V1	•	•	•	o	•	•
V2	•	o	•	•	•	•
V3	•	•	•	•	•	•
V4	•	•	o	•	•	•
V5	•	•	•	•	•	•
V6	•	•	•	•	•	•
V7	•	o/• Alternates with V23	•	o/• Alternates with V23	•	•
V8	•	•	•	•	•	•
V9	•	o	o	•	•	•
V10	•	•	•	•	•	•
V11	•	o/• Pump In	o/• Pump In/ Pump Out	o/• Pump In	o/• Pump In	•

plasma and up to about 250 ml of red blood cells. This procedure will, in shorthand, be called the red blood cell/plasma collection procedure.

The portion of the red blood cells not retained for collection are periodically returned to the donor during blood separation. Plasma collected in excess of the 550 ml target and red blood cells collected in excess of the 250 ml target are also returned to the donor at the end of the procedure.

Programming of the blood processing circuit 46 (through the selective application of pressure to the valves and pump stations of the cassette) makes it possible to use the same universal set 264 used to carry out the double red blood cell collection or the plasma collection procedure.

The procedure includes a pre-collection cycle, a collection cycle, and a post-collection cycle, and a storage preparation cycle.

During the pre-collection cycle, the set 264 is primed to vent air prior to venipuncture. During the collection cycle, whole blood drawn from the donor is processed to collect plasma and red blood cells, while returning a portion of the red blood cells to the donor. During the post-collection cycle, excess plasma and red blood cells are returned to the donor, and the set is flushed with saline. During the storage preparation cycle, a red blood cell storage solution added to the collected red blood cells.

(1) The Pre-Collection Cycle

a. Anticoagulant Prime

In the pre-collection cycle for the red blood cell / plasma collection procedure, the cassette is programmed to carry out AC Prime 1 and AC Prime 2 Phases that are identical to the AC Prime 1 and AC Prime 2 Phases of the double red blood cell collection procedure.

b. Saline Prime

In the pre-collection cycle for the red blood cell /

Phase	AC Prime 1	AC Prime 2	Saline Prime 1	Saline Prime 2	Saline Prime 3	Vent Donor Line	Veni-puncture
V12	●	●	●	●	o (Stage 1) o/● Pump In (Stage 2)	●	●
V13	o/● Pump In	o	●	●	●	o/● Pump Out	●
V14	●	●	o/● Pump In	o/● Pump In	o/● Pump Out (Stage 1) o (Stage 2)	●	●
V15	o	o/● Pump In Pump Out	●	●	●	o	●
V16	●	●	●	●	●	●	●
V17	●	●	●	●	●	●	●
V18	o	o	●	●	●	o	●
V19	o	o	●	●	●	o	●
V20	o	o/● Pump Out Pump In	●	●	●	o	●
V21	●	●	●	●	●	●	●
V22	●	●	o	o	o	●	●
V23	●	●	o	o	o	●	●
PP1	■	■	□	□	□ (Stage 1)	■	■
PP2	■	■	■	■	□ (Stage 2)	■	■
PP3	□	■	■	■	■	□	■
PP4	■	□	■	■	■	■	■

Caption: o denotes an open valve; ● denotes a closed valve;

circuit is programmed to enter a phase (Blood Separation Without Whole Blood Draw) to terminate operation of the donor interface pump station PP3 (while also closing valves V13, V11, V18, and V13) to terminate collection of whole blood in the in-process container 312, while still continuing blood separation. If the volume of whole blood reaches a predetermined minimum threshold in the in-process container 312 during blood separation, but before the targeted volume of either plasma or red blood cells is collected, the circuit is programmed to return to the Blood Separation With Whole Blood Draw, to thereby refill the in-process container 312. The circuit is programmed to toggle between the Blood Separation cycle with whole blood draw and without whole blood draw according to the high and low volume thresholds for the in-process container 312, until the requisite maximum volumes of plasma and red blood cells have been collected.

c. Return Red Blood Cells and Saline

If the targeted volume of plasma has not been collected, and red blood cells collected in the red blood cell container 308 exceed a predetermined maximum threshold, the next phase of the blood collection cycle (Return Red Blood Cells With Separation) programs the blood processing circuit 46 to operate the donor interface pump station PP3 (i.e., in through valve V11 and out through valve V13); the in-process pump PP1 (i.e., in through valve V9 and out through valve V14); and the plasma pump PP2 (i.e., in through valve V12 and out through valve V10). This arrangement continues to convey anticoagulated whole blood from the in-process container 312 into the processing chamber for separation, while removing plasma into the plasma container 304 and red blood cells into the red blood cell container 308. This arrangement also conveys all or a portion of the red blood cells collected in the red blood cell container 308 to the donor. This arrangement also

valve V13) to draw whole blood from the in process container 312 to fill the donor tube 266, thereby purge red blood cells (mixed with saline) in preparation for another draw whole blood cycle.

The circuit is then programmed to conduct another Blood Separation While Drawing Whole Blood Phase, to refill the in process container 312. If required, the circuit is capable of performing successive draw whole blood and return red blood cells cycles, until the weigh sensors indicate that volumes of red blood cells and plasma collected in the containers 304 and 308 are at or somewhat greater than the targeted values. The post-collection cycle then commences.

The programming of the circuit during the phases of the collection cycle is summarized in the following table.

TABLE

Programming of Blood Processing Circuit During The Collection Cycle

(Red Blood Cell / Plasma Collection Procedure)

Phase	Blood Prime 1	Blood Prime 2	Blood Separation While Drawing Whole Blood (Without Drawing Whole Blood)	Return Red Blood Cells / Saline with Separation (Without Separation)	Fill Donor Line
V1	•	•	•	•	o
V2	•	•	o	o	•
V3	o	•	o (•)	•	•
V4	•	•	•	•	•
V5	•	•	o	o (•)	•
V6	•	•	•	•	•
V7	•	o	•	o/• Alternates with V23	o
V8	•	•	•	•	•

Phase	Blood Prime 1	Blood Prime 2	Blood Separation While Drawing Whole Blood (Without Drawing Whole Blood)	Return Red Blood Cells / Saline with Separation (Without Separation)	Fill Donor Line
PP2	■	■	□	□ (■)	■
PP3	□	■	□ (■)	□	□
PP4	□	■	□ (■)	■	■

Caption: o denotes an open valve; ● denotes a closed valve; o/● denotes a valve opening and closing during a pumping sequence; ■ denotes an idle pump station (not in use); and □ denotes a pump station in use.

d. The Post-Collection Cycle

Once the targeted maximum volumes of plasma and red blood cells have been collected (as monitored by the weigh sensor), the circuit is programmed to carry out the phases of the post-collection cycle.

i. Return Excess Plasma

If the volume of plasma collected in the plasma collection container 304 is over the targeted volume, a phase of the post-collection cycle (Excess Plasma Return) is entered, during which the circuit is programmed to terminate the supply and removal of blood to and from the processing chamber, while operating the donor interface pump station PP3 (i.e., in through valve V11 and out through valve V13) to convey plasma in the plasma container 304 to the donor. The circuit is also programmed in this phase to mix saline from the container 288 in line with the returned plasma. This phase continues until the volume of plasma in the plasma collection container 304 is at the targeted value, as monitored by the weigh sensor.

continues until the in-process container 312 is empty, as monitored by the weigh sensor.

In the next phase (Fluid Replacement), the circuit is programmed to operate the donor interface pump station PP3 (i.e., in through valve V11 and out through valve V13) to convey the saline to the donor. This phase continues until a prescribed replacement volume amount is infused, as monitored by the weigh sensor.

In the next phase (End Venipuncture), the circuit is programmed to close all valves and idle all pump stations, so that venipuncture can be terminated.

The programming of the circuit during the phases of the post-collection cycle is summarized in the following table.

TABLE

Programming of Blood Processing Circuit During The Post-Collection Cycle

(Red Blood Cell / Plasma Collection Procedure)

Phase	Excess Plasma Return	Excess RBC Return	Saline Purge	Final Return	Fluid Replace-ment	End Veni-puncture
V1	•	•	•	o	•	•
V2	•	o	•	•	•	•
V3	•	•	•	•	•	•
V4	•	•	o	•	•	•
V5	o	•	•	•	•	•
V6	o/• Alternates with V23	•	•	•	•	•
V7	•	o/• Alternates with V23	•	o/• Alternates with V23	•	•
V8	•	•	•	•	•	•
V9	o	o	o	•	•	•
V10	•	•	•	•	•	•

In the first phase of the storage preparation cycle (Prime Storage Solution), the circuit is programmed to operate the donor interface pump station PP3 to transfer a desired volume of red blood cell storage solution from the container 280 into the in-process container 312. The transfer of the desired volume is monitored by the weigh scale.

In the next phase (Transfer Storage Solution), the circuit is programmed to operate the donor interface pump station PP3 to transfer a desired volume of red blood cell storage solution from the in-process container 312 into the red blood cell collection container 308. The transfer of the desired volume is monitored by the weigh scale.

In the next and final phase (End Procedure), the circuit is programmed to close all valves and idle all pump stations, so that the plasma and red blood cell storage containers 304 and 308 can be separated and removed for storage. The remainder of the disposable set can now be removed and discarded.

The programming of the circuit during the phases of the storage preparation cycle is summarized in the following table.

TABLE

Programming of Blood Processing Circuit During The Storage Preparation Cycle

(Red Blood Cell / Plasma Collection Procedure)

Phase	Prime Storage Solution	Transfer Storage Solution	End Procedure
V1	•	•	•
V2	•	o	•
V3	o	•	•
V4	•	o	•
V5	•	•	•
V6	•	•	•

and a region of plasma (see Fig. 15A). The centrifugal forces cause the region of packed red blood cells to congregate along the outside or high-G wall of the chamber, while the region of plasma is transported to the inside or low-G wall of the chamber.

An intermediate region forms an interface between the red blood cell region and the plasma region. Intermediate density cellular blood species like platelets and leukocytes populate the interface, arranged according to density, with the platelets closer to the plasma layer than the leukocytes. The interface is also called the "buffy coat," because of its cloudy color, compared to the straw color of the plasma region and the red color of the red blood cell region.

It is desirable to monitor the location of the buffy coat, either to keep the buffy coat materials out of the plasma or out of the red blood cells, depending on the procedure, or to collect the cellular contents of the buffy coat. The system includes a sensing station 332 comprising two optical sensors 334 and 336 for this purpose.

In the illustrated and preferred embodiment (see Fig. 13), the sensing station 332 is located a short distance outside the centrifuge station 20. This arrangement minimizes the fluid volume of components leaving the chamber before monitoring by the sensing station 332.

The first sensor 334 in the station 332 optically monitors the passage of blood components through the plasma collection tube 292. The second sensor 336 in the station 332 optically monitors the passage of blood components through the red blood cell collection tube 294.

The tubes 292 and 294 are made from plastic (e.g. polyvinylchloride) material that is transparent to the optical energy used for sensing, at least in the region where the tubes 292 and 294 are to be placed into association with the sensing station 332.

components that are optically targeted for detection vary depending upon the procedure.

For a plasma collection procedure, the first sensor 334 detects the presence of platelets in the plasma collection tube 292, so that control measures can be initiated to move the interface between the plasma and platelet cell layer back into the processing chamber. This provides a plasma product that can be essentially platelet-free or at least in which the number of platelets is minimized.

For a red blood cell-only collection procedure, the first sensor 334 detects the interface between the buffy coat and the red blood cell layer, so that control measures can be initiated to move this interface back into the processing chamber. This maximizes the red blood cell yield.

For a buffy coat collection procedure (which will be described later), the first sensor 334 detects when the leading edge of the buffy coat (i.e., the plasma/platelet interface) begins to exit the processing chamber, as well as detects when the trailing edge of the buffy coat (i.e., the buffy coat / red blood cell interface) has completely exited the processing chamber.

The presence of these cellular components in the plasma, as detected by the first sensor 334, indicates that the interface is close enough to the low-G wall of the processing chamber to allow all or some of these components to be swept into the plasma collection line (see Fig. 15B). This condition will also be called an "over spill."

The second sensor 336 is capable of detecting the hematocrit of the red blood cells in the red blood cell collection tube 294. The decrease of red blood hematocrit below a set minimum level during processing that the interface is close enough to the high-G wall of the processing chamber to allow plasma to enter the red blood cell collection tube 294 (see Fig. 15C). This condition will

Ambient light typically contains frequency components less than 1000 Hz, and EMI typically contains frequency components above 2 Khz. With this in mind, the modulator 346 modulates the current at a frequency below the EMI frequency components, e.g., at about 2 Khz. The bandpass filter 364 has a center frequency of about the same value, i.e., about 2 Khz. The sensor circuit 340 eliminates frequency components above and below the ambient light source and EMI components from the sensed measurement. In this way, the sensing circuit 340 is not sensitive to ambient lighting conditions and EMI.

More particularly, transmitted or reflected light from the tube 292 or 294 containing the fluid to be measured is incident on photodiodes 354 and 355 (for the tube 292) or photodiodes 358 and 360 (for tube 294). Each photodiode produces a photocurrent proportional to the received light intensity. This current is converted to a voltage. The voltage is fed, via the multiplexer 370, to the bandpass filter 364. The bandpass filter 364 has a center frequency at the carrier frequency of the modulated source light (i.e., 2 Khz in the illustrated embodiment).

The sinusoidal output of the bandpass filter 364 is sent to the variable gain amplifier 366. The gain of the amplifier is preprogrammed in preestablished steps, e.g., X1, X10, X100, and X1000. This provides the amplifier with the capability to respond to a large dynamic range.

The sinusoidal output of the amplifier 366 is sent to the full wave rectifier 368, which transforms the sinusoidal output to a DC output voltage proportional to the transmitted light energy.

The controller 16 generates timing pulses for the sensor circuit 340. The timing pulses comprise, for each LED, (i) a modulation square wave at the desired modulation frequency (i.e., 2Khz in the illustrated embodiment), (ii) an enable signal, (iii) two sensor select bits (which select

for red blood cells.

In the illustrated embodiment, the first sensor 334 includes an emitter 350 of light at a first wavelength (λ_1), which, in the illustrated embodiment, is green light (570 nm and 571 nm). The first sensor 334 also includes an emitter 352 of light at a second wavelength (λ_2), which, in the illustrated embodiment, is red light (645 nm to 660 nm).

The optical attenuation for platelets at the first wavelength ($\varepsilon_{platelets}{}^{\lambda}{}_1$) and the optical attenuation for platelets at the second wavelength ($\varepsilon_{platelets}{}^{\lambda}{}_2$) are generally the same. Thus, changes in attenuation over time, as affected by increases or decreases in platelet concentration, will be similar.

However, the optical attenuation for hemoglobin at the first wavelength ($\varepsilon_{Hb}{}^{\lambda}{}_1$) is about ten times greater than the optical attenuation for hemoglobin at the second wavelength ($\varepsilon_{Hb}{}^{\lambda}{}_2$). Thus, changes in attenuation over time, as affected by the presence of red blood cells, will not be similar.

The tube 294, through which plasma to be sensed, is transparent to light at the first and second wavelengths. The tube 294 conveys the plasma flow past the first and second emitters 350 and 352.

The light detector 354 receives light emitted by the first and second emitters 350 and 352 through the tube 294. The detector 354 generates signals proportional to intensities of received light. The intensities vary with optical attenuation caused by the presence of platelets and/or red blood cells.

The module 372 is coupled to the light detector 354 to analyze the signals to derive intensities of the received light at the first and second wavelengths. The module 372 compares changes of the intensities of the first and second wavelengths over time. When the intensities of the first and second wavelengths change over time in substantially the same manner, the module 372 generates an output representing

cells and platelets at the applied wavelengths, as well as the measurement geometry.

For wavelengths in the visible and near infrared spectrum, $\varepsilon_{platelets}^{\lambda} \approx 0$, therefore:

$$Ln(\frac{I^{\lambda}}{I_0^{\lambda}}) = Ln(T^{\lambda}) \approx -[(\varepsilon_{Hb}^{\lambda} C_{Hb} H)d + G_{platelets}^{\lambda} + G_{RBC}^{\lambda}] \quad (2)$$

In an over spill condition (shown in Fig. 15B), the first cellular component to be detected by the first sensor 334 in the plasma collection line 294 will be platelets. Therefore, for the detection of platelets, $Ln(T^{\lambda}) \approx G_{platelets}^{\lambda}$.

To detect the buffy coat interface between the platelet layer and the red blood cell layer, the two wavelengths (λ_1 and λ_2) are chosen based upon the criteria that (i) λ_1 and λ_2 have approximately the same path length factor (G^{λ}), and (ii) one wavelength λ_1 or λ_2 has a much greater optical attenuation for hemoglobin than the other wavelength.

Assuming the wavelengths λ_1 and λ_2 have the same G^{λ}, Equation (2) reduces to:

$$Ln(T^{\lambda_1}) - Ln(T^{\lambda_2}) \approx Hdc_{Hb}(\varepsilon_{Hb}^{\lambda_2} - \varepsilon_{Hb}^{\lambda_1}) \quad (3)$$

In the preferred embodiment, λ_1 = 660 nm (green) and λ_2 = 571 nm (red). The path length factor (G^{λ}) for 571 nm light is greater than for 660 nm light. Therefore the path length factors have to be modified by coefficients α and β, as follows: :

$$G_{RBC}^{\lambda_1} = \alpha G_{RBC}^{\lambda_2}$$
$$G_{platelets}^{\lambda_1} = \beta G_{platelets}^{\lambda_2}$$

Therefore, Equation (3) can be reexpressed as follows:

$$Ln(T^{\lambda_1}) - Ln(T^{\lambda_2}) \approx Hdc_{Hb}(\varepsilon_{Hb}^{\lambda_2} - \varepsilon_{Hb}^{\lambda_1}) + (\alpha - 1)G_{RBC}^{\lambda_2} + (\beta - 1)G_{platelets}^{\lambda_2} \quad (4)$$

In the absence of red blood cells, Equation (3) causes a false red blood cell detect with increasing platelet concentrations, as Equation (5) demonstrates:

quality of red blood cells that are collected for storage.

In either situation, the ability to sense when an under spill condition exists is desireable.

Photon wavelengths in the near infrared spectrum (NIR) (approximately 540 nm to 1000 nm) are suitable for sensing red blood cells, as their intensity can be measured after transmission through many millimeters of blood.

The sensor circuit 340 includes a red blood cell detection module 374. The detection module 374 analyses sensed optical transmissions of the second sensor 336 to discern the hematocrit and changes in the hematocrit of red blood cells exiting the processing chamber 18.

The detection module 374 considers that the attenuation of a beam of monochromatic light of wavelength λ by blood may be described by the modified Lambert-Beer law, as follows:

$$I = I_O e^{-[(\varepsilon^{\lambda}_{Hb} c_{Hb} H)d + G^{\lambda}_{RBC}]} \qquad (6)$$

where:

I is transmitted light intensity.

I_o is incident light intensity.

$\varepsilon_{Hb}^{\lambda}$ is the extinction coefficient of hemoglobin (Hb) (gm/dl) at the applied wavelength.

C_{Hb} is the concentration of hemoglobin in a red blood cell, taken to be 34 gm/dl.

d is the distance between the light source and light detector.

G^{λ} is the path length factor at the applied wavelength, which accounts for additional photon path length in the media due to light scattering.

H is whole blood hematocrit, which is percentage of red blood cells in the sample.

G_{RBC}^{λ} is a function of the hematocrit and scattering coefficients of red blood cells at the applied wavelengths, as well as the measurement geometry.

can treat the optical density of the sample for the reflected light to be a linear function of hematocrit. The same relationship exists for the first sensor 334 with respect to the detection of red blood cells in plasma.

This arrangement relies upon maintaining straightforward measurement geometries. No mirrors or focusing lenses are required. The LED or photodiode need not be positioned at an exact angle with respect to the blood flow tube. No special optical cuvettes are required. The second sensor 336 can interface directly with the transparent plastic tubing 294. Similarly, the first sensor 334 can interface directly with the transparent tubing 292.

In the illustrated embodiment, the wavelength 805 nm is selected, as it is an isobestic wavelength for red blood cells, meaning that light absorption by the red blood cells at this wavelength is independent of oxygen saturation. Still, other wavelengths can be selected within the NIR spectrum.

In the illustrated embodiment, for a wavelength of 805 nm, the preferred set distance is 7.5 mm from the light source. The fixture 338, above described (see Fig. 18), facilitates the placement of the tube 294 in the desired relation to the light source and the reflected light detector of the second sensor 336. The fixture 338 also facilitates the placement of the tube 292 in the desired relation to the light source and the reflected light detector of the first sensor 334.

Measurements at a distance greater than 7.5 mm can be made and will show a greater sensitivity to changes in the red blood cell hematocrit. However a lower signal to noise ratio will be encountered at these greater distances. Likewise, measurements at a distance closer to the light source will show a greater signal to noise ratio, but will be less sensitive to changes in the red blood cell hematocrit. The optimal distance for a given wavelength in

292 is set at a fraction (e.g., 80%) of the desired plasma flow rate (Q_p) from the processing chamber 18, to purge saline from the chamber 18. The purge of saline continues under these conditions until the first sensor 334 optically senses the presence of saline in the plasma collection line 292.

1. For Plasma Collection Procedures (Induced Under Spill)

If the procedure to be performed collects plasma for storage (e.g., the Plasma Collection Procedure or the Red Blood Cell / Plasma Collection Procedure), an under spill condition is induced during calibration. The under spill condition is created by decreasing or stopping the flow of plasma through the plasma collection line 292. This forces the buffy coat away from the low-G side of the chamber 18 (as Fig. 15C) to assure that a flow of "clean" plasma exists in the plasma collection line 292, free or essentially free of platelets and leukocytes. The induced under spill allows the first sensor 334 to be calibrated and normalized with respect to the physiologic color of the donor's plasma, taking into account the donor's background lipid level, but without the presence of platelets or leukocytes. The first sensor 334 thereby possesses maximum sensitivity to changes brought about by the presence of platelets or leukocytes in the buffy coat, should an over spill subsequently occur during processing.

Forcing an under spill condition also positions the interface close to the high-G wall at the outset of blood processing. This creates an initial offset condition on the high-G side of the chamber, to prolong the ultimate development of an over spill condition as blood processing proceeds.

2. Red Blood Cell Collection Procedures

If a procedure is to be performed in which no plasma is to be collected (e.g., the Double Unit Red Blood Cell

higher hematocrit than in a traditional plasma collection procedure.

The system controller 16 maintains the pump settings until the desired plasma collection volume is achieved, unless an under spill condition or an over spill condition is detected.

If set Q_p is too high for the actual blood separation conditions, or, if due to the physiology of the donor, the buffy coat volume is larger (i.e., "thicker") than expected, the first sensor 334 will detect the presence of platelets or leukocytes, or both in the plasma, indicating an over spill condition.

In response to an over spill condition caused by a high Q_p, the system controller 16 terminates operation of the plasma collection pump PP2, while keeping set Q_{WB} unchanged. In response to an over spill condition caused by a high volume buffy coat, the system controller 16 terminates operation of the plasma collection pump PP2, until an under spill condition is detected by the red blood cell sensor 336. This serves to expel the buffy coat layer from the separation chamber through the red blood cell tube 294.

To carry out the over spill response, the blood processing circuit 46 is programmed to operate the in-process pump PP1 (i.e., drawing in through the valve V9 and expelling out of the valve V14), to draw whole blood from the in-process container 312 into the processing chamber 18 at the set Q_{WB}. Red blood cells exit the chamber 18 through the tube 294 for collection in the collection container 308. The flow rate of red blood cells directly depends upon the magnitude of Q_{WB}.

During this time, the blood processing circuit 46 is also programmed to cease operation of the plasma pump PP2 for a preestablished time period (e.g., 20 seconds). This forces the interface back toward the middle of the separation chamber. After the preestablished time period, the operation

V20	•
V21	•
V22	•
V23	•
PP1	□
PP2	■
PP3	■
PP4	■

Caption: o denotes an open valve; • denotes a closed valve; o/• denotes a valve opening and closing during a pumping sequence; ■ denotes an idle pump station (not in use); and □ denotes a pump station in use.

Upon correction of an over spill condition, the controller 16 returns the blood processing circuit 46 to resume normal blood processing, but applies a percent reduction factor (%RF) to the Q_p set at the time the over spill condition was initially sensed. The reduction factor (%RF) is a function of the time between over spills, i.e., %RF increases as the frequency of over spills increases, and vice versa.

If set Q_p is too low, the second sensor 336 will detect a decrease in the red blood cell hematocrit below a set level, which indicates an under spill condition.

In response to an under spill condition, the system controller 16 resets Q_p close to the set Q_{WB}. As processing continues, the interface will, in time, move back toward the low-G wall. The controller 16 maintains these settings until the second sensor 336 detects a red blood cell hematocrit above the desired set level. At this time, the controller 16 applies a percent enlargement factor (%EF) to the Q_p set at the time the under spill condition was initially sensed. The enlargement factor (%EF) is a function of the time between under spills, i.e., %EF increases as the frequency of under

blood cells detected in the tube 292 are thereby returned to the processing chamber 18, and are thereby prevented from entering the plasma collection container 304.

The interface will, in time, move back toward the high-G wall. The controller 16 maintains these settings until the second sensor 336 detects a decrease in the red blood cell hematocrit below a set level, which indicates an under spill condition.

In response to an under spill condition, the system controller 16 increases Q_p until the second sensor 336 detects a red blood cell hematocrit above the desired set level. At this time, the controller 16 resets Q_p to the value at the time the most recent overspill condition was sensed.

3. Buffy Coat Collection

If desired, an over spill condition can be periodically induced during a given plasma collection procedure to collect the buffy coat in a buffy coat collection container 376 (see Fig. 10). As Fig. 10 shows, in the illustrated embodiment, the buffy coat collection container 376 is coupled by tubing 378 to the buffy port P4 of the cassette 28. The buffy coat collection container 376 is suspended on a weigh scale 246, which provides output reflecting weight changes over time, from which the controller 16 derives the volume of buffy coat collected.

In this arrangement, when the induced over spill condition is detected, the blood processing circuit 46 is programmed (through the selective application of pressure to the valves and pump stations) to operate the plasma pump PP2 (i.e., drawing in through valve V12 and expelling out through valve V10), to draw plasma from the processing chamber 18 through the tube 378, while valves V4 and V6 are closed and valve V8 is opened. The buffy coat in the tube 378 is conveyed into the buffy coat collection container 376. The blood processing circuit 46 is also programmed during this time to operate the in-process pump PP1 (i.e., drawing in

V21	•
V22	•
V23	•
PP1	□
PP2	□
PP3	■
PP4	■

Caption: ○ denotes an open valve; • denotes a closed valve; ○/• denotes a valve opening and closing during a pumping sequence; ■ denotes an idle pump station (not in use); and □ denotes a pump station in use.

After a prescribed volume of buffy coat is conveyed into the buffy coat collection container 376 (as monitored by the weigh scale 246), normal blood processing conditions are resumed. Over spill conditions causing the movement of the buffy coat into the tube 378 can be induced at prescribed intervals during the process period, until a desired buffy coat volume is collected in the buffy coat collection container.

VI. Another Programmable Blood Processing Circuit

A. Circuit Schematic

As previously mentioned, various configurations for the programmable blood processing circuit 46 are possible. Fig. 5 schematically shows one representative configuration 46, the programmable features of which have been described. Fig. 34 shows another representative configuration of a blood processing circuit 46' having comparable programmable features.

Like the circuit 46, the circuit 46' includes several pump stations PP(N), which are interconnected by a pattern of fluid flow paths F(N) through an array of in line valves V(N). The circuit is coupled to the remainder of the blood processing set by ports P(N).

The circuit 46' includes a programmable network of flow

stations. In one representative embodiment, the draw cycle is ten seconds, and the expel cycle is one second. The expelling pump station performs its one second cycle at the beginning of the draw cycle of the drawing pump, and then rests for the remaining nine seconds of the draw cycle. The pump stations then switch draw and expel functions. This creates a continuous inlet flow and a pulsatile outlet flow. The provision of two alternating pump stations PP3 and PP4 serves to reduce overall processing time, as fluid is continuously conducted into a drawing pump station through out the procedure.

In this arrangement, the isolated pump station PP5 of the circuit 46' serves as a dedicated anticoagulant pump, like pump station PP4 in the circuit 46, to draw anticoagulant from a source through the port P10 and to meter anticoagulant into the blood through port P9.

In this arrangement, as in the circuit 46, the universal pump station PP1 serves, regardless of the particular blood processing procedure performed, as a dedicated in-process whole blood pump, to convey whole blood into the blood separator. As in the circuit 46, the dedicated function of the pump station PP1 frees the donor interface pumps PP3 and PP4 from the added function of supplying whole blood to the blood separator. Thus, the in-process whole blood pump PP1 can maintain a continuous supply of blood to the blood separator, while the donor interface pumps PP3 and PP4 operate in tandem to simultaneously draw and return blood to the donor through the single phlebotomy needle. The circuit 46' thus minimizes processing time.

In this arrangement, as in circuit 46, the universal pump station PP2 of the circuit 46' serves, regardless of the particular blood processing procedure performed, as a plasma pump, to convey plasma from the blood separator. As in the circuit 46, the ability to dedicate separate pumping functions in the circuit 46' provides a continuous flow of

connection, to thereby maintain a sterile, closed blood processing environment.

Tubes 290', 292', and 294', extend to an umbilicus 296' which is coupled to the processing chamber 18'. The tubes 290', 292', and 294 are coupled, respectively, to the ports P5, P6, and P7. The tube 290' conveys whole blood into the processing chamber 18 under the operation of the in-process pump station PP1. The tube 292' conveys plasma from the processing chamber 18' under the operation of the plasma pump chamber PP2. The tube 294' conveys red blood cells from processing chamber 18'.

A plasma collection container 304' is coupled by a tube 302' to the port P3. The collection container 304' is intended, in use, to serve as a reservoir for plasma during processing.

A red blood cell collection container 308' is coupled by a tube 306' to the port P2. The collection container 308' is intended, in use, to receive a unit of red blood cells for storage.

A buffy coat collection container 376' is coupled by a tube 377' to the port P4. The container 376' is intended, in use, to receive a volume of buffy coat for storage.

A whole blood reservoir 312' is coupled by a tube 310' to the port P1. The collection container 312' is intended, in use, to receive whole blood during operation of the donor interface pumps PP3 and PP4, to serve as a reservoir for whole blood during processing. It can also serve to receive a second unit of red blood cells for storage.

B. The Cassette

As Figs. 35 and 36 show, the programmable fluid circuit 46' can be implemented as an injection molded, pneumatically controlled cassette 28'. The cassette 28' interacts with the pneumatic pump and valve station 30, as previously described, to provide the same centralized, programmable, integrated platform as the cassette 28.

serves to trap air in the flow path to and from the donor.

Another interior cavity 201' (see Fig. 35) is also provided in the back side 192' of the cassette body 188'. The cavity 201' is placed in the circuit 46' between the port P5 and the valve V16 of the in-process pumping station PP1. Blood enters the cavity 201' from flow path F16 through opening 203' and exits the cavity 201' into flow path F5 through opening 205' The cavity 201' serves as another air trap within the cassette body 188' in the flow path serving the separation chamber 26'. The cavity 201' also serves as a capacitor to dampen the pulsatile pump strokes of the in-process pump PP1 serving the separation chamber.

C. Associated Pneumatic Manifold Assembly

Fig. 43 shows a pneumatic manifold assembly 226' that can be used in association with the cassette 28', to supply positive and negative pneumatic pressures to convey fluid through the cassette 28'. The front side 194' of the diaphragm is held in intimate engagement against the manifold assembly 226' when the door 32 of the pump station 20 is closed and bladder 314 inflated. The manifold assembly 226', under the control of the controller 16, selectively distributes the different pressure and vacuum levels to the pump and valve actuators PA(N) and VA(N) of the cassette 28'. These levels of pressure and vacuum are systematically applied to the cassette 28', to route blood and processing liquids. Under the control of a controller 16, the manifold assembly 226 also distributes pressure levels to the door bladder 314 (already described), as well as to a donor pressure cuff (also already described) and to a donor line occluder 320 (also already described). The manifold assembly 226' for the cassette 28' shown in Fig. 43 shares many attributes with the manifold assembly 226 previously described for the cassette 28, as shown in Fig. 12.

Like the manifold assembly 226, the manifold assembly 226' is coupled to a pneumatic pressure source 234', which

drive the expression of liquid from the donor interface pumps PP3 and PP4 and the anticoagulant pump PP5.

Vhard, or Hard Vacuum (-350 mmHg), is the deepest vacuum applied in the manifold assembly 226' to open cassette valves V1 to V25. Vgen, or General Vacuum (-300 mmHg), is applied to drive the draw function of each of the pumps PP1 to PP5. Vgen is required to be less extreme than Vhard, to ensure that pumps PP1 to PP5 do not overwhelm upstream and downstream cassette valves V1 to V25.

A main hard pressure line 322' and a main vacuum line 324' distribute Phard and Vhard in the manifold assembly 324. The pressure and vacuum sources 234' run continuously to supply Phard to the hard pressure line 322' and Vhard to the hard vacuum line 324'. A pressure sensor S2 monitors Phard in the hard pressure line 322'. The sensor S2 opens and closes the solenoid 38 to build Phard up to its maximum set value.

Similarly, a pressure sensor S6 in the hard vacuum line 324' monitors Vhard. The sensor S6 controls a solenoid 43 to maintain Vhard as its maximum value.

A general pressure line 326' branches from the hard pressure line 322'. A sensor S4 in the general pressure line 326' monitors Pgen. The sensor S2 controls a solenoid 34 to maintain Pgen within its specified pressure range.

A general vacuum line 330' branches from the hard vacuum line 324'. A sensor S5 monitors Vgen in the general vacuum line 330'. The sensor S5 controls a solenoid 45 to keep Vgen within its specified vacuum range.

In-line reservoirs R1 to R4 are provided in the hard pressure line 322, the general pressure line 326', the hard vacuum line 324', and the general vacuum line 330'. The reservoirs R1 to R4 assure that the constant pressure and vacuum adjustments as above described are smooth and predictable.

The solenoids 32 and 43 provide a vent for the

cassette 28' to perform all the various blood process functions already described. Certain pumping functions for the fluid circuit 46', common to various blood processing procedures, will be described by way of example.

1. Whole Blood Flow To the In-Process Container

In a first phase of a given blood collection cycle, the blood processing circuit 46' is programmed (through the selective application of pressure to the valves and pump stations of the cassette 28') to jointly operate the donor interface pumps PP3 and PP4 to transfer anticoagulated whole blood into the in-process container 312' prior to separation.

In a first phase (see Fig. 37A), the pump PP3 is operated in a ten second draw cycle(i.e., in through valves V12 and V13, with valves V6, V14, V18, and V15 closed) in tandem with the anticoagulant pump PP5 (i.e., in through valve V22 and out through valve V21) to draw anticoagulated blood through the donor tube 270 into the pump PP3. At the same time, the donor interface pump PP4 is operated in a one second expel cycle to expel (out through valve V7) anticoagulant blood from its chamber into the process container 312' through flow paths F20 and F1(through opened valve V4).

At the end of the draw cycle for pump PP3 (see Fig. 37B), the blood processing circuit 46' is programmed to operate the donor interface pump PP4 in a ten second draw cycle(i.e., in through valves V12 and V14, with valves V13, V18, and V18 closed) in tandem with the anticoagulant pump PP5 to draw anticoagulated blood through the donor tube 270 into the pump PP4. At the same time, the donor interface pump PP3 is operated in a one second expel cycle to expel (out through valve V6) anticoagulant blood from its chamber into the process container 312' through the flow paths F20 and F1 (through opened valve V4).

These alternating cycles continue until an incremental volume of anticoagulated whole blood enters the in process

At the end of the draw cycle for pump PP3 (see Fig. 37E), the blood processing circuit 46' is programmed to operate the donor interface pump PP4 in a ten second draw cycle(i.e., in through valve V7, with valves V6 and V14 closed) to draw red blood cells from the red blood cell container 308' into the pump PP4. At the same time, the donor interface pump PP3 is operated in a one second expel cycle to expel (out through valves V13 and V18, with valve V12 closed) red blood cells from its chamber to the donor through the filter chamber 200'. These alternating cycles continue until a desired volume of red blood cells are returned to the donor.

Simultaneously, valves V24, V20, and V8 are opened, so that the drawing pump station PP3 or PP4 also draws saline from the saline container 288' for mixing with red blood cells drawn into the chamber. As before explained, the in line mixing of saline with the red blood cells raises the saline temperature and improves donor comfort, while also lowering the hematocrit of the red blood cells.

Simultaneously, the in-process pump PP1 is operated (i.e., in through valve V1 and out through valve V16) and the plasma pump PP2 (i.e., in through valve V17 and out through valve V11, with valve V9 open) to convey anticoagulated whole blood from the in-process container 312 into the processing chamber for separation, while removing plasma into the plasma container 304, in the manner previously described with respect to the fluid circuit 46.

3. In-Line Addition of Red Blood Cell Additive Solution

In a blood processing procedure where red blood cells are collected for storage (e.g., the Double Red Blood Cell Collection Procedure or the Red Blood Cell and Plasma Collection Procedure) the circuit 46' is programmed to operate the donor interface pump station PP3 in a ten second draw cycle(in through valves V15 and V13, with valve V23

valves V18 and V8 closed and valves V15 and V25 opened) to expel red blood cells through tube 291' through the in-line leukocyte depletion filter 293' to the leukocyte-depleted red blood cell storage container 289'.

At the end of the draw cycle for pump PP3 (see Fig. 39B), the blood processing circuit 46' is programmed to operate the donor interface pump PP4 in a ten second draw cycle(i.e., in through valve V7, with valves V14 and V18 closed) to draw red blood cells from the container 312' or 308' into the pump PP4. At the same time, the donor interface pump PP3 is operated in a one second expel cycle to expel (out through valve V13, with valve V12 closed and valves V15 and V25 opened) red blood cells through tube 291' through the in-line leukocyte depletion filter 293' to the leukocyte-depleted red blood cell storage container 289'. These alternating cycles continue until a desired volume of red blood cells are transfered through the filter 293 into the container 289'.

5. Staged Buffy Coat Harvesting

In circuit 46 (see Fig. 5), buffy coat is collected through port P4, which is served by flow line F4, which branches from flow line F26, which conveys plasma from the plasma pump station PP2 to the plasma collection container 304 (also see Fig. 10). In the circuit 46' (see Fig. 34), the buffy coat is collected through the port P4 from the flow path F6 as controlled by valve V19. The buffy coat collection path bypasses the plasma pump station PP2, keeping the plasma pump station PP2 free of exposure to the buffy coat, thereby keeping the collected plasma free of contamination by the buffy coat components.

During separation, the system controller (already described) maintains the buffy coat layer within the separation chamber 18' at a distance spaced from the low-G wall, away from the plasma collection line 292 (see Fig. 15A). This allows the buffy coat component to accumulate

assembly 226' can include an auxiliary pneumatic actuator A_{AUX} selectively apply P_{HARD} to the region of the flexible diaphragm that overlies the interior cavity 201' (see Fig. 35). As previously described, whole blood expelled by the pumping station PP1 (by application of P_{HARD} by actuator PA2), enters flow path F5 through openings 203' and 205' into the processing chamber 18'. During the next subsequent stroke of the PP1, to draw whole blood into the pumping chamber PP1 by application of V_{GEN} by actuator PA2, residual whole blood residing in the cavity 201' is expelled into flow path F5 through opening 205', and into the processing chamber 18' by application of P_{HARD} by A_{AUX}. The cavity 201' also serves as a capacitor to dampen the pulsatile pump strokes of the in-process pump PP1 serving the separation chamber 18'.

It is desirable to conduct seal integrity testing of the cassette 28' shown in Fig. 35 and 36 prior to use. The integrity test determines that the pump and valve stations within the cassette 28' function without leaking. In this situation, it is desirable to isolate the cassette 28' from the separation chamber 26'. Valves V19 and V16 (see Fig. 34) in circuit 264' provide isolation for the whole blood inlet and plasma lines 292' and 296' of the chamber 18'. To provide the capability of also isolating the red blood cell line 294', an extra valve fluid actuated station V26 can be added in fluid flow path F7 serving port P7. As further shown in phantom lines in Fig. 43, an addition valve actuator VA26 can be added to the manifold assembly 26', to apply positive pressure to the valve V26, to close the valve V26 when isolation is required, and to apply negative pressure to the valve V26, to open the valve when isolation is not required.

VII. Blood Separation Elements

A. Molded Processing Chamber

Figs. 21 to 23 show an embodiment of the centrifugal processing chamber 18, which can be used in association with the system 10 shown in Fig. 1.

As seen in Fig. 23, the inside annular wall 122 is open between one pair 130 of the stiffening walls. The opposing stiffening walls form an open interior region 134 in the hub 120, which communicates with the channel 126. Blood and fluids are introduced from the umbilicus 296 into and out of the separation channel 126 through this region 134.

In this embodiment (as Fig. 23 shows), a molded interior wall 136 formed inside the region 134 extends entirely across the channel 126, joining the outside annular wall 124. The wall 136 forms a terminus in the separation channel 126, which interrupts flow circumferentially along the channel 126 during separation.

Additional molded interior walls divide the region 124 into three passages 142, 144, and 146. The passages 142, 144, and 146 extend from the hub 120 and communicate with the channel 126 on opposite sides of the terminus wall 136. Blood and other fluids are directed from the hub 120 into and out of the channel 126 through these passages 142, 144, and 146. As will be explained in greater detail later, the passages 142, 144, and 146 can direct blood components into and out of the channel 126 in various flow patterns.

The underside of the base 388 (see Fig. 22) includes a shaped receptacle 179. Three preformed nipples 180 occupy the receptacle 179. Each nipple 180 leads to one of the passages 142, 144, 146 on the opposite side of the base 388.

The far end of the umbilicus 296 includes a shaped mount 178 (see Figs. 24 and 24A). The mount 178 is shaped to correspond to the shape of the receptacle 179. The mount 178 can thus be plugged into the receptacle 179 (as Fig. 25 shows). The mount 178 includes interior lumens 398 (see Fig. 24A), which slide over the nipples 180 in the hub 120, to couple the umbilicus 296 in fluid communication with the channel 126.

Ribs 181 within the receptacle 179 (see Fig. 22) uniquely fit within a key way 183 formed on the mount 178

yoke 154 having bottom, top, and side walls 156, 158, 160. The yoke 154 spins on a bearing element 162 attached to the bottom wall 156. An electric drive motor 164 is coupled via an axle to the bottom wall 156 of the collar 154, to rotate the yoke 154 about an axis 64. In the illustrated embodiment, the axis 64 is tilted about fifteen degrees above the horizontal plane of the base 38, although other angular orientations can be used.

A rotor plate 166 spins within the yoke 154 about its own bearing element 168, which is attached to the top wall 158 of the yoke 154. The rotor plate 166 spins about an axis that is generally aligned with the axis of rotation 64 of the yoke 154.

The top of the processing chamber 18 includes an annular lip 380, to which the lid 150 is secured. Gripping tabs 382 carried on the periphery of the rotor plate 166 make snap-fit engagement with the lip 380, to secure the processing chamber 18 on the rotor plate 166 for rotation.

A sheath 182 on the near end of the umbilicus 296 fits into a bracket 184 in the centrifuge station 20. The bracket 184 holds the near end of the umbilicus 296 in a non-rotating stationary position aligned with the mutually aligned rotational axes 64 of the yoke 154 and rotor plate 166.

An arm 186 protruding from either or both side walls 160 of the yoke 154 contacts the mid portion of the umbilicus 296 during rotation of the yoke 154. Constrained by the bracket 184 at its near end and the chamber 16 at its far end (where the mount 178 is secured inside the receptacle 179), the umbilicus 296 twists about its own axis as it rotates about the yoke axis 64. The twirling of the umbilicus 296 about its axis as it rotates at one omega with the yoke 154 imparts a two omega rotation to the rotor plate 166, and thus to the processing chamber 18 itself.

The relative rotation of the yoke 154 at a one omega rotational speed and the rotor plate 166 at a two omega

buffy coat into the red blood cell collection passage 144 (creating an over spill condition). The recessed exit channel 386 thereby permits red blood cell yields to be maximized (in a red blood cell collection procedure) or an essentially platelet-free plasma to be collected (in a plasma collection procedure).

In an alternative flow arrangement (see Fig. 30), the umbilicus 296 conveys whole blood into the channel 126 through the passage 142. The processing chamber 18 rotates (arrow R in Fig. 30) in the same direction as whole blood flow (which is clockwise in Fig. 30). Alternatively, the chamber 18 can be rotated in a direction opposite to the circumferential flow of whole blood, i.e., clockwise. The whole blood separates as a result of centrifugal forces in the manner shown in Fig. 15A. Red blood cells are driven toward the high-G wall 124, while lighter plasma constituent is displaced toward the low-G wall 122.

In this flow pattern, the dam 384 (previously described) prevents passage of plasma, while allowing passage of red blood cells into the recessed channel 386. The channel 386 directs the red blood cells into the umbilicus 296 through the radial passage 144. The plasma constituent is conveyed from the opposite end of the channel 126 through the radial passage 146 into umbilicus 296.

In another alternative flow arrangement (see Fig. 31), the umbilicus 296 conveys whole blood into the channel 126 through the passage 144. The processing chamber 18 is rotated (arrow R in Fig. 31) in the same direction as blood flow (which is clockwise in Fig. 31). Alternatively, the chamber 18 can be rotated in a direction opposite to the circumferential flow of whole blood, i.e., counterclockwise. The whole blood separates as a result of centrifugal forces in the manner shown in Fig. 15A. Red blood cells are driven toward the high-G wall 124, while lighter plasma constituent is displaced toward the low-G wall 122.

described will occur in either circumstance. Nevertheless, it has been discovered that, rotating the chamber 18 in the same direction as the flow of whole blood in the channel 126 during separation, appears to minimize disturbances due, e.g., Coriolis effects, resulting in increased separation efficiencies.

Example

Whole blood was separated during various experiments into red blood cells and plasma in processing chambers 18 like that shown in Fig. 28. In one chamber (which will be called Chamber 1), whole blood circumferentially flowed in the channel 126 in the same direction as the chamber 18 was rotated (i.e., the chamber 18 was rotated in a counterclockwise direction). In the other chamber 18 (which will be called Chamber 2), whole blood circumferentially flowed in the channel 126 in a direction opposite to chamber rotation (i.e., the chamber 18 was rotated in a clockwise direction). The average hematocrit for red blood cells collected were measured for various blood volume samples, processed at different combinations of whole blood inlet flow rates and plasma outlet flow rates. The following Tables summarize the results for the various experiments.

Table 1

(Flow in the Same Direction as Rotation)

	Average Whole Blood Hematocrit (%)	Average Hematocrit of Red Blood Cells Collected
Number of Blood Samples Processed		
7	45.4	74.8
4	40	78.8

Table 2

(Flow in the Opposite Direction as Rotation)

and 390 at their opposite ends.

As the processing chamber 18' rotates (arrow R in Fig. 33), the umbilicus 296 conveys whole blood into the outside channel 126' through the passage 144'. The whole blood flows in the channel 126' in the same direction as rotation (which is counterclockwise in Fig. 33). Alternatively, the chamber 18' can be rotated in a direction opposite to the circumferential flow of whole blood, i.e., clockwise. The whole blood separates in the outside channel 126' as a result of centrifugal forces in the manner shown in Fig. 15A. Red blood cells are driven toward the high-G wall 124', while lighter plasma constituent is displaced toward the low-G wall 122'.

As previously described, the dam 384' prevents passage of plasma, while allowing passage of red blood cells into a channel 386' recessed in the high-G wall 124'. The channel 386' directs the red blood cells into the umbilicus 296 through the radial passage 142'. The plasma constituent is conveyed from the channel 126' through the interruption 394 into the inside separation channel 390.

The plasma flows circumferentially flow through the inside channel 390 in a direction opposite to the whole blood in the outside channel 126'. Platelets remaining in the plasma migrate in response to centrifugal forces against the annular wall 124'. The channel 390 directs the plasma constituent to the same end of the chamber 18' where whole blood is initially introduced. The plasma constituent is conveyed from the channel 390 by the passage 146'.

VIII. Other Blood Processing Functions

The many features of the invention have been demonstrated by describing their use in separating whole blood into component parts for storage and blood component therapy. This is because the invention is well adapted for use in carrying out these blood processing procedures. It should be appreciated, however, that the features of the

We Claim:

1. A blood processing system comprising

a donor flow channel to convey fluid to and from a donor,

a blood processing flow channel including a blood separation chamber to separate a blood component from donor blood,

a blood component collection flow channel including a blood component collection container,

a pump station communicating with the donor flow channel, the blood processing flow channel, and the blood component collection flow channel, and

a controller to operate the pump station in multiple modes, including a processing mode, during which the pump station is operated to convey blood in the donor flow channel into the blood processing flow channel for separation of the blood component in the blood separation chamber, and a collection mode, during which the pump station is operated to convey at least some of the blood component in the blood processing flow channel into the blood component collection flow channel for collection in the blood component collection container.

2. A system according to claim 1

wherein the blood component collection flow channel includes a filter to remove undesired materials from the blood component before entering the blood component collection container.

3. A system according to claim 2

wherein the filter removes leukocytes.

4. A system according to claim 1

wherein the controller operates the pump station in a blood component return mode, during which the pump station is operated to convey at least some of the blood component in the blood processing flow channel into the donor flow channel for return to the donor.

further including an actuator to receive the cassette and operate the pump station, and

wherein the controller is coupled to the actuator.

12. A system according to claim 1

wherein the blood processing flow channel includes a blood component holding container to hold the blood component, and

wherein, in the collection mode, the pump station is operated to convey at least some of the blood component in the blood component holding container into the blood component collection flow channel.

13. A system according to claim 12

wherein the controller operates the pump station in a blood component return mode, during which the pump station is operated to convey at least some of the blood component in the blood component holding container into the donor flow channel for return to the donor.

14. A system according to claim 1

wherein the blood processing flow channel includes a donor blood holding container to hold donor blood prior to separation in the blood separation chamber, and

wherein, in the processing mode, the pump station is operated to convey blood in the donor flow channel into the donor blood holding container.

15. A system according to claim 14

further including a second pump station, independent of the first defined pump station, communicating with the donor blood holding container and the blood separation chamber and operating to convey donor blood from the donor blood holding container in the blood separation chamber for separation in the blood component.

16. A system according to claim 1

wherein the pump station comprises first and second fluid pressure actuated pump stations, and

pump station is operated to convey whole blood in the donor flow channel into the blood processing flow channel for separation of the red blood cells in the blood separation chamber, and a collection mode, during which the pump station is operated to convey at least some of the red blood cells in the blood processing flow channel into the blood component collection flow channel for on-line removal of leukocytes and collection in the red blood cell collection container.

20. A system according to claim 19

wherein the controller operates the pump station in a blood component return mode, during which the pump station is operated to convey at least some of the red blood cells in the blood processing flow channel into the donor flow channel for return to the donor.

21. A system according to claim 19

further including a utility flow channel including a processing fluid container,

wherein the pump station communicates with the utility flow channel, and

wherein the controller operates the pump station during the blood component return mode to convey processing fluid in the utility flow channel into the donor flow channel for mixing with the red blood cells returned to the donor.

22. A system according to claim 21

wherein the processing fluid includes saline.

23. A system according to claim 19

further including a utility flow channel including a processing fluid container,

wherein the pump station communicates with the utility flow channel, and

wherein the controller operates the pump station in a processing fluid transfer mode, during which the pump station is operated to convey processing fluid in the utility flow channel into the blood processing flow channel for mixing with the red blood cells.

fluid flow to the destination is pulsatile.

29. A blood processing method comprising the steps of

coupling a multi-function pump station to a donor flow channel to convey fluid to and from a donor, a blood processing flow channel including a blood separation chamber to separate a blood component from donor blood, and a blood component collection flow channel including a blood component collection container, and

operating the pump station in multiple modes, including a processing mode, during which the pump station is operated to convey blood in the donor flow channel into the blood processing flow channel for separation of the blood component in the blood separation chamber, and a collection mode, during which the pump station is operated to convey at least some of the blood component in the blood processing flow channel into the blood component collection flow channel for collection in the blood component collection container.

30. A method according to claim 29

wherein, in operating the pump station in the collection mode, the blood component is passed through an in-line filter in the blood component collection flow channel to remove undesired materials from the blood component before entering the blood component collection container.

31. A method according to claim 30

wherein the filter removes leukocytes.

32. A method according to claim 29

further including operating the pump station in a blood component return mode, during which the pump station is operated to convey at least some of the blood component in the blood processing flow channel into the donor flow channel for return to the donor.

33. A method according to claim 29

further including coupling the pump station to a

a fluid volume from the second pump station to the destination, and a second flow state, in which the pump strokes draw a fluid volume into the second pump station from the source and expel a fluid volume from the first pump station to the destination, the control function operating to synchronize the pump strokes so that fluid flow from the source is essentially continuous while fluid flow to the destination is pulsatile.

40. A red blood cell processing method comprising the steps of

coupling a multi-function pump station to a donor flow channel to convey fluid to and from a donor, a blood processing flow channel including a blood separation chamber to separate red blood cells from donor whole blood, and a blood component collection flow channel including a red blood cell collection container and an in-line filter to remove leukocytes from the red blood cells before entering the red blood cell collection container,

operating the pump station in multiple modes, including a processing mode, during which the pump station is operated to convey whole blood in the donor flow channel into the blood processing flow channel for separation of the red blood cells in the blood separation chamber, and a collection mode, during which the pump station is operated to convey at least some of the red blood cells in the blood processing flow channel into the blood component collection flow channel for on-line removal of leukocytes and collection in the red blood cell collection container.

41. A method according to claim 40

further including operating the pump station in a blood component return mode, during which the pump station is operated to convey at least some of the red blood cells in the blood processing flow channel into the donor flow channel for return to the donor.

42. A method according to claim 40

the source and expel a fluid volume from the first pump station to the destination, the control function operating to synchronize the pump strokes so that fluid flow from the source is essentially continuous while fluid flow to the destination is pulsatile.

FIG. 2

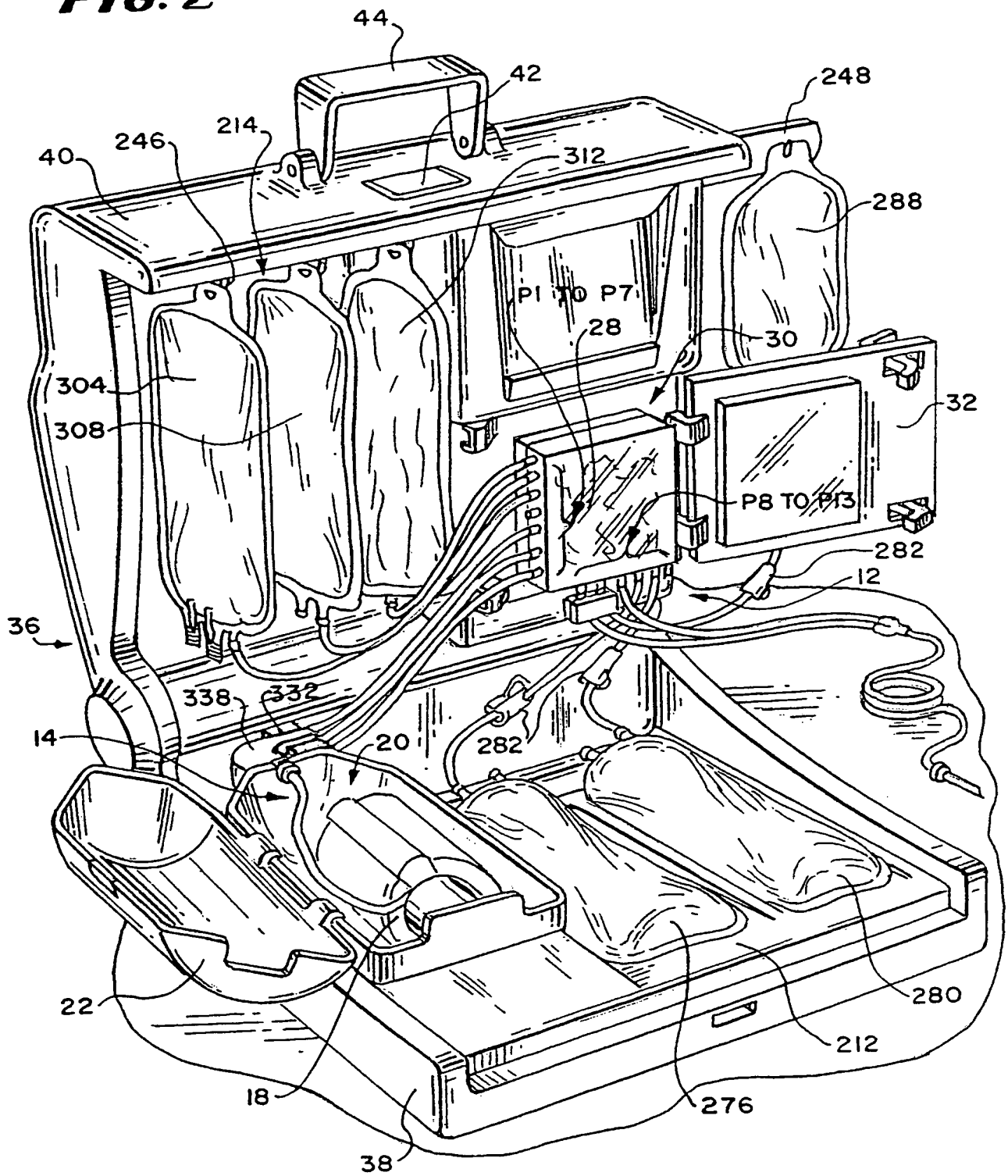
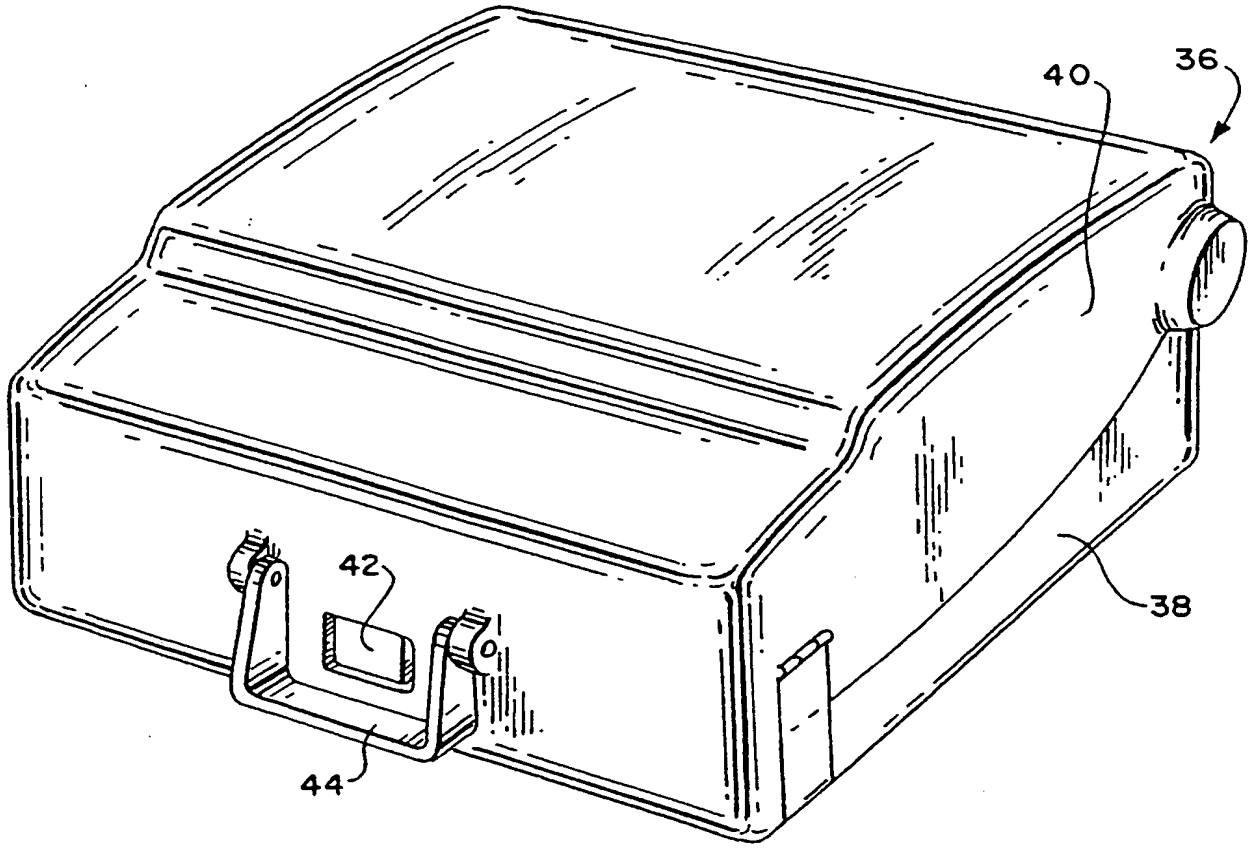

44
42
248
214
246
40
312
288
P1 TO P7
28
30
304
32
308
P8 TO P13
282
12
36
338
332
14
20
282
280
22
212
18
276
38

FIG. 4



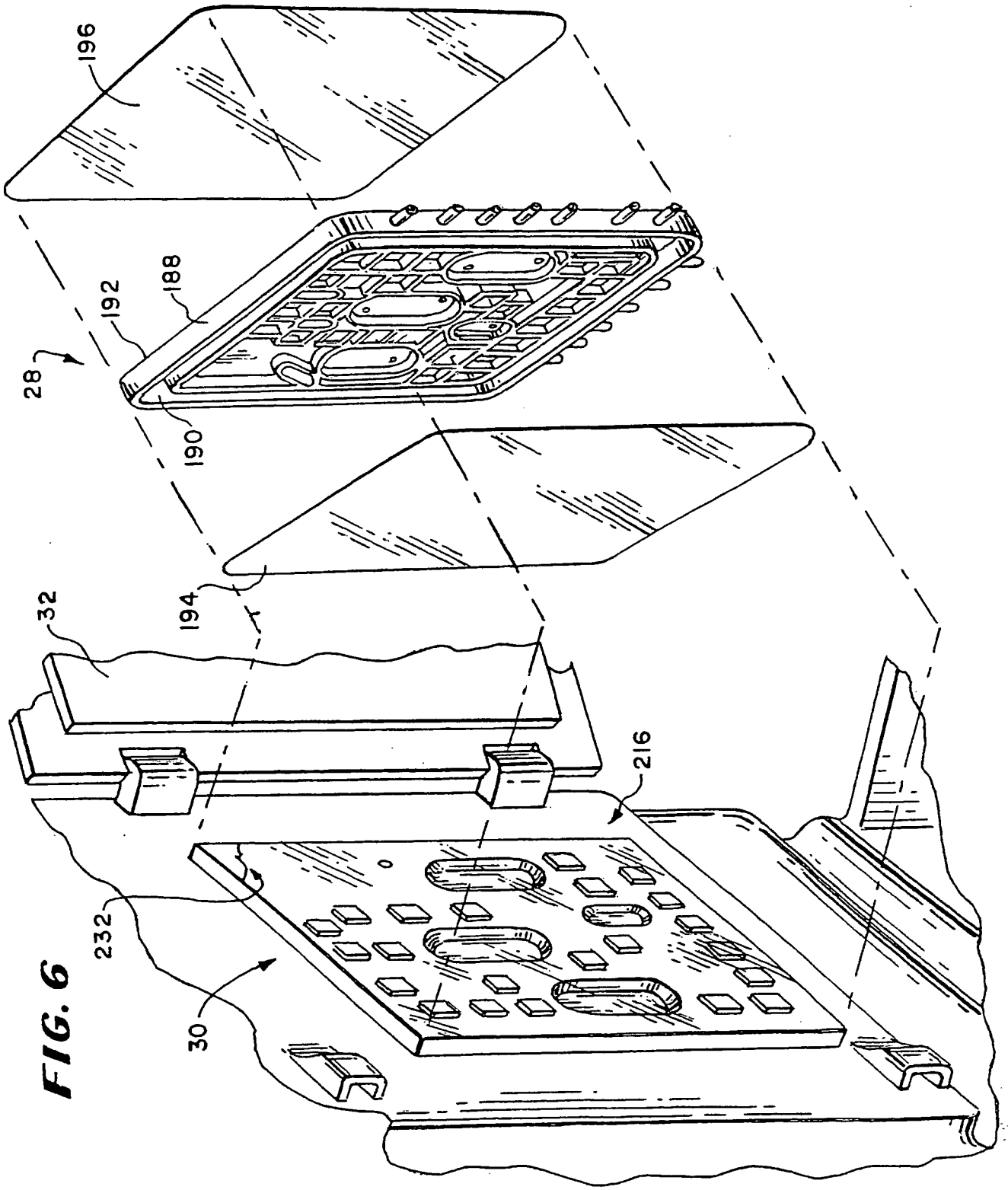
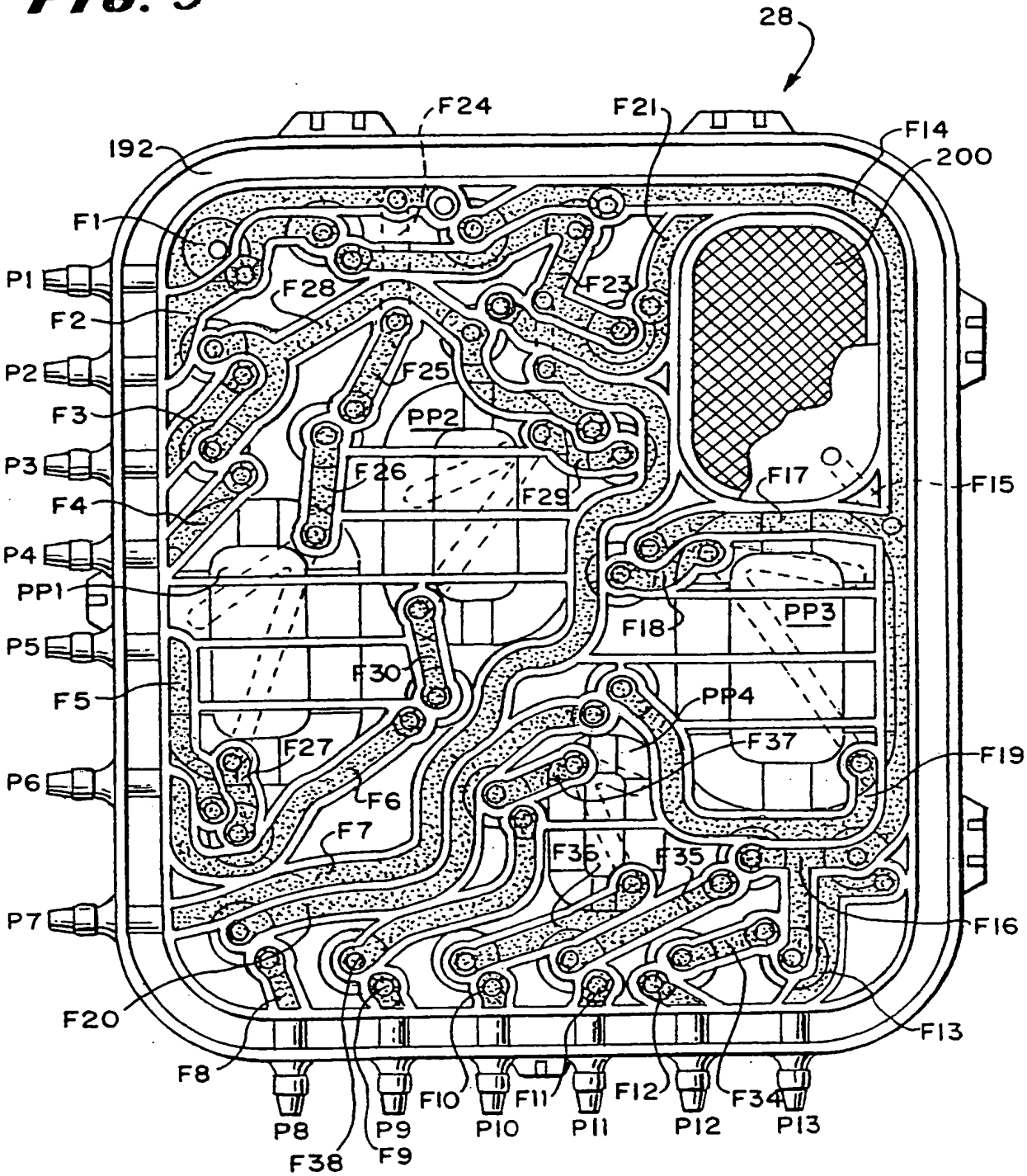


FIG. 6

FIG. 9



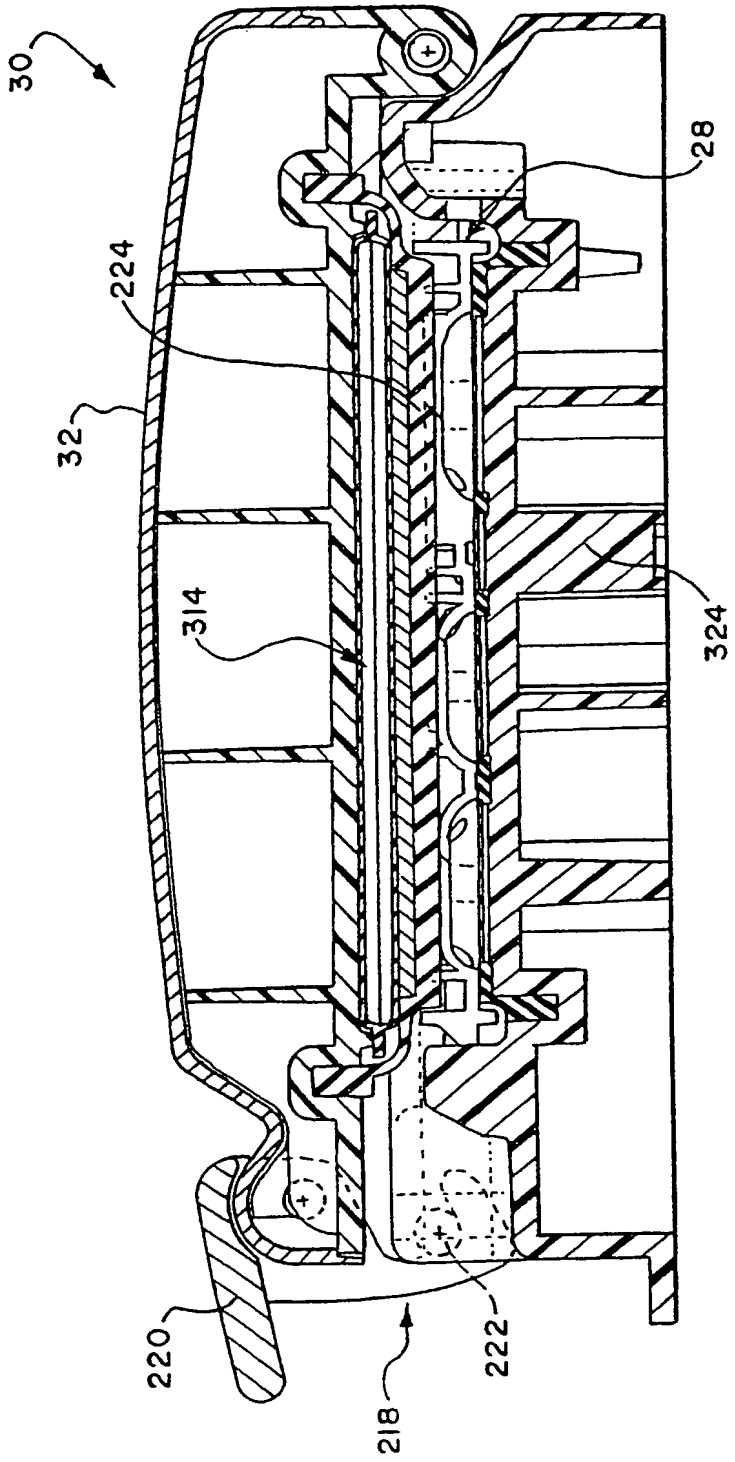


FIG. 11

FIG. 13

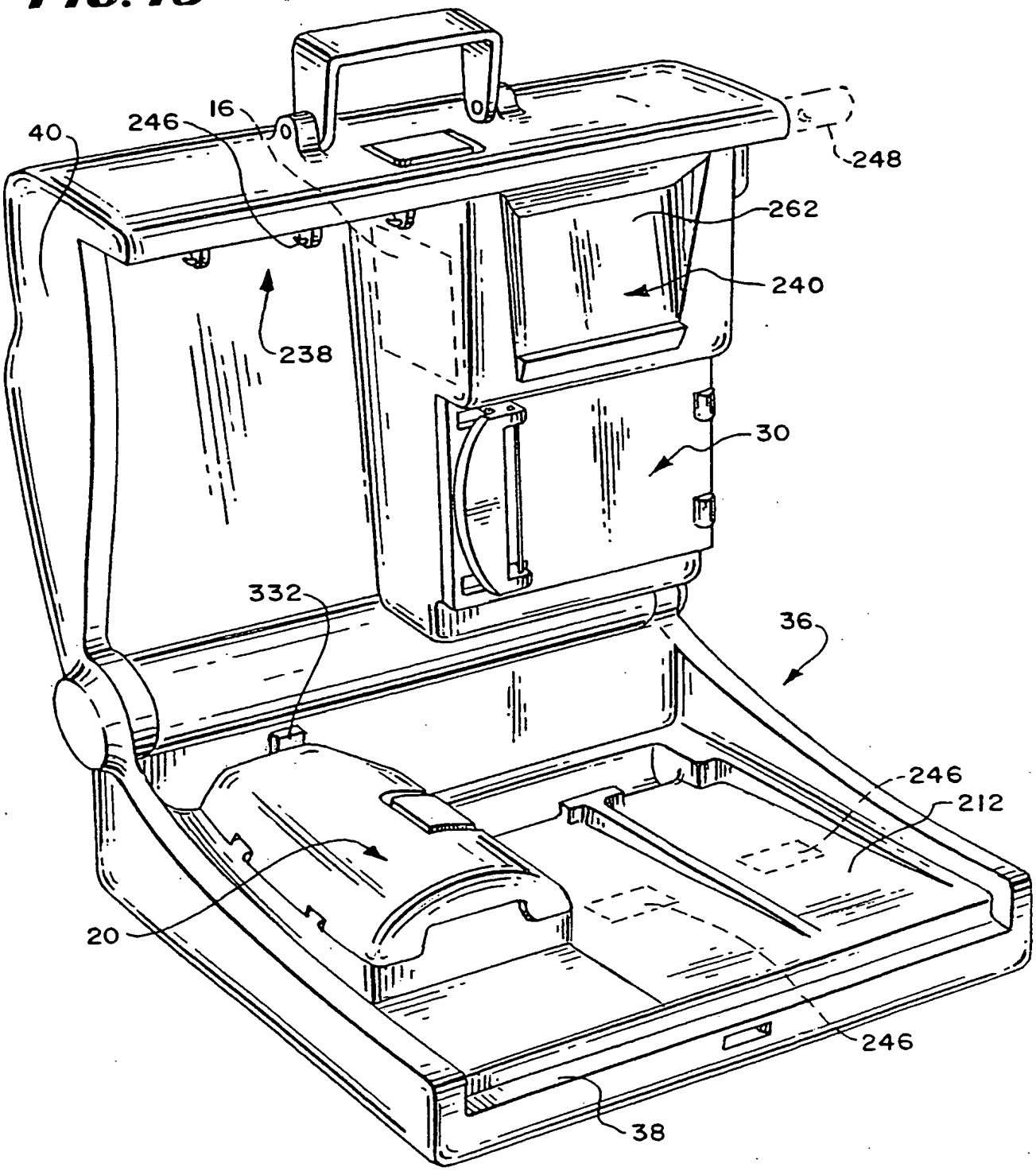


FIG. 15A

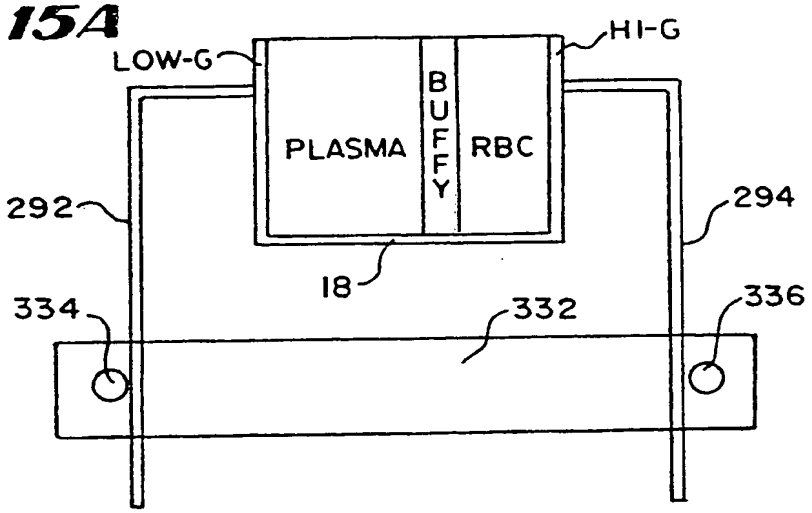


FIG. 15B

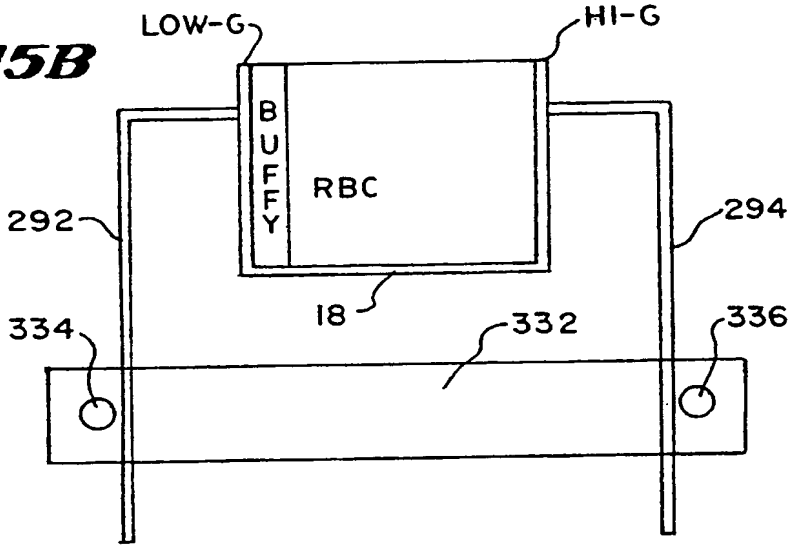
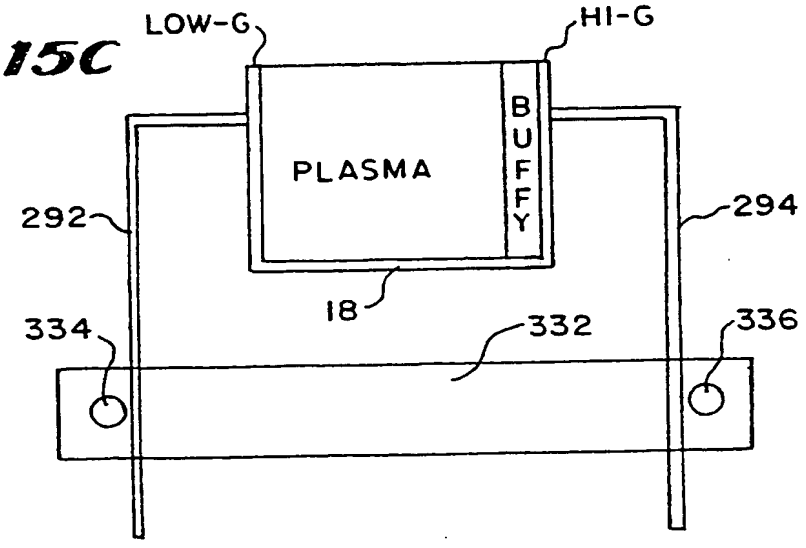


FIG. 15C



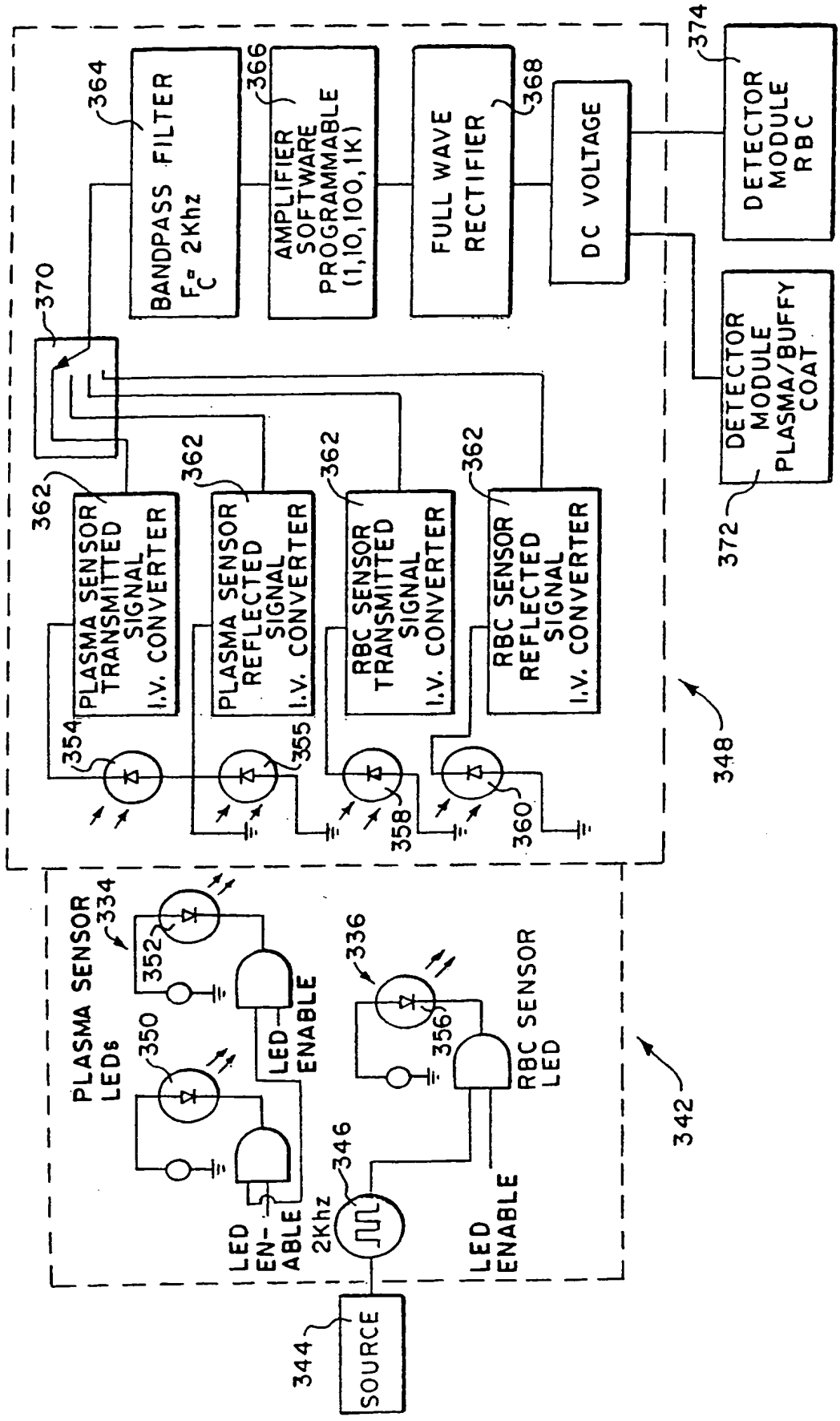


FIG. 19

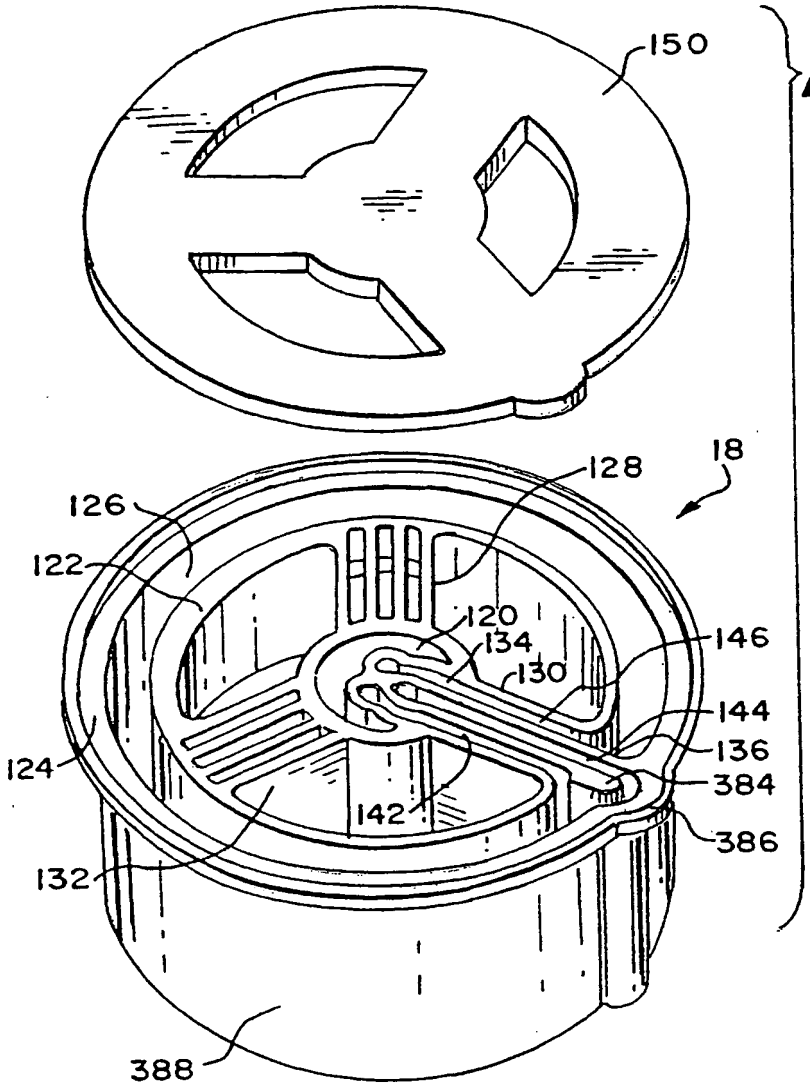


FIG. 21

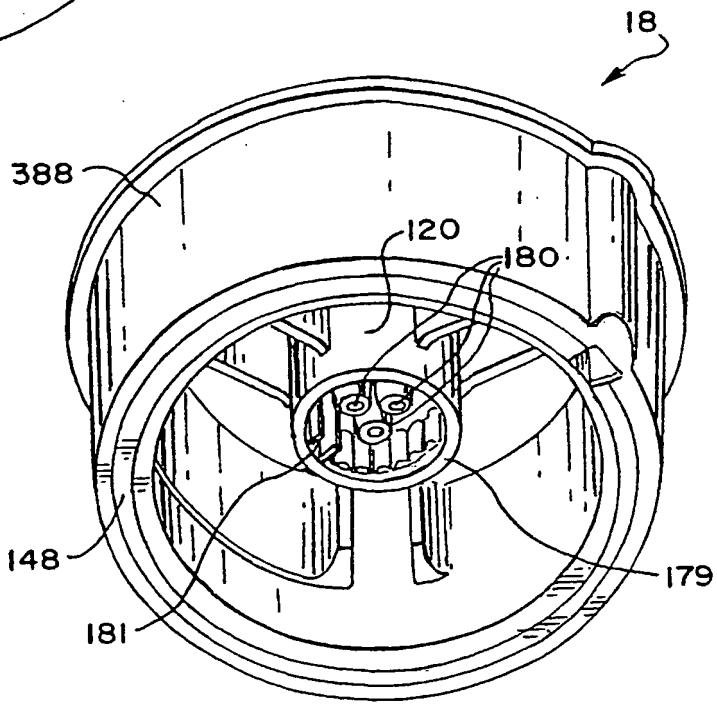
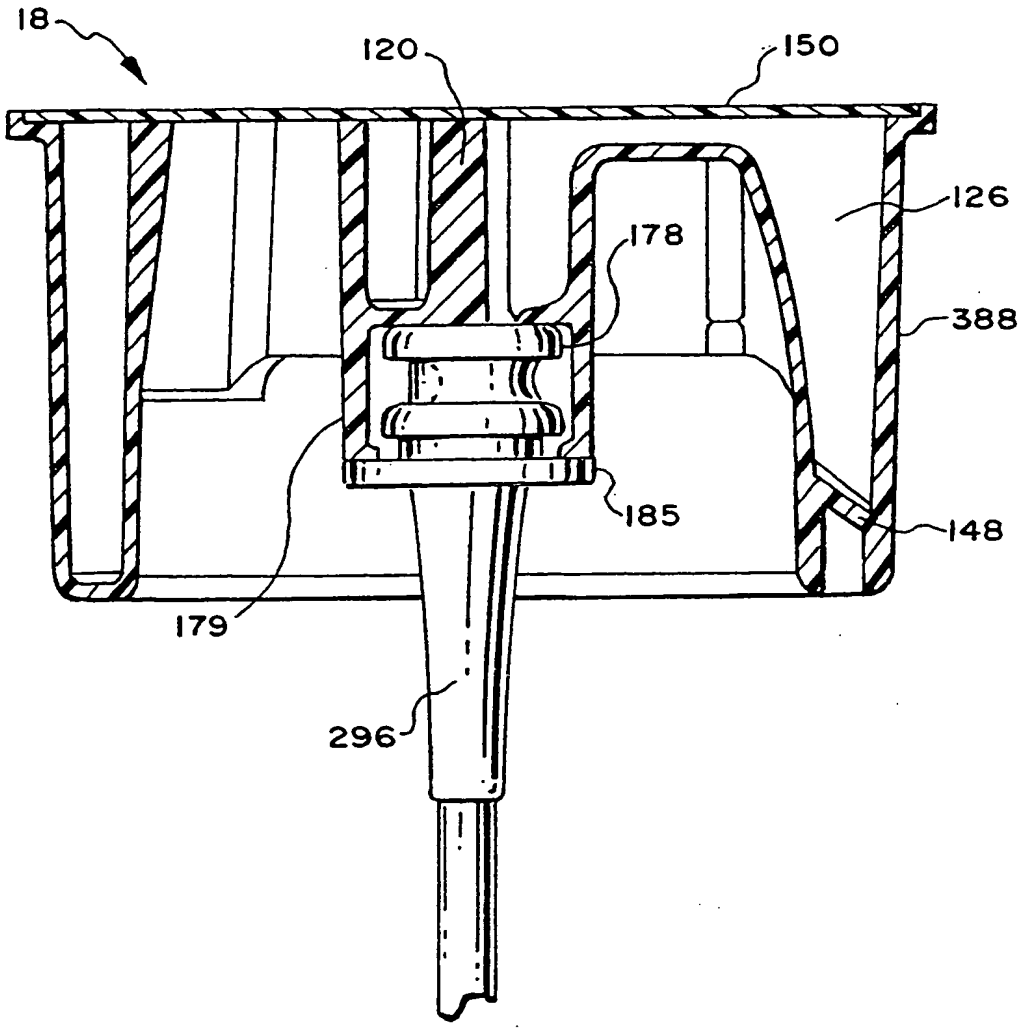


FIG. 22

FIG. 25



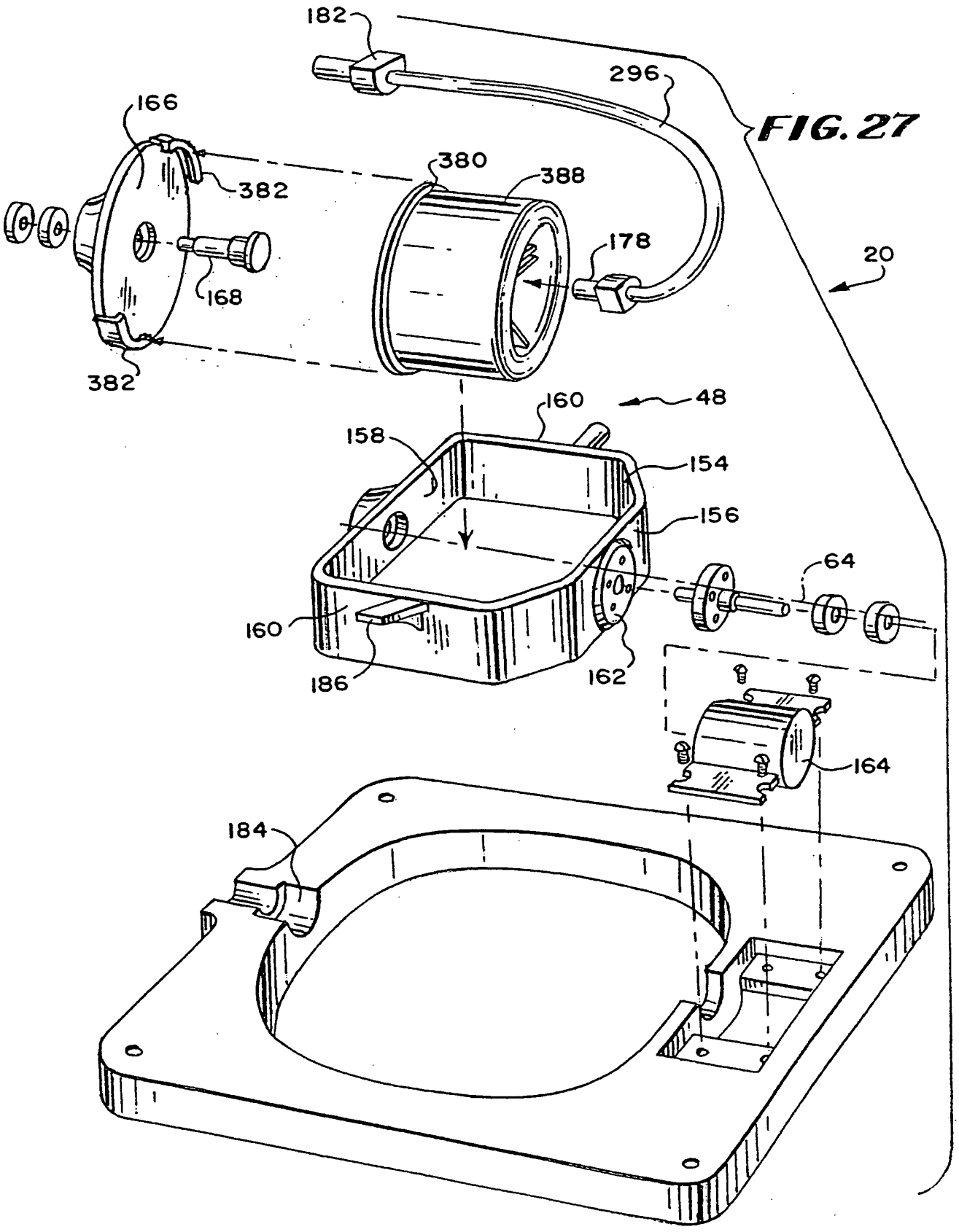

182
296
166
380
388
382
178
168
20
382
160
48
158
154
156
64
160
186
162
164
184

FIG. 27

FIG. 29

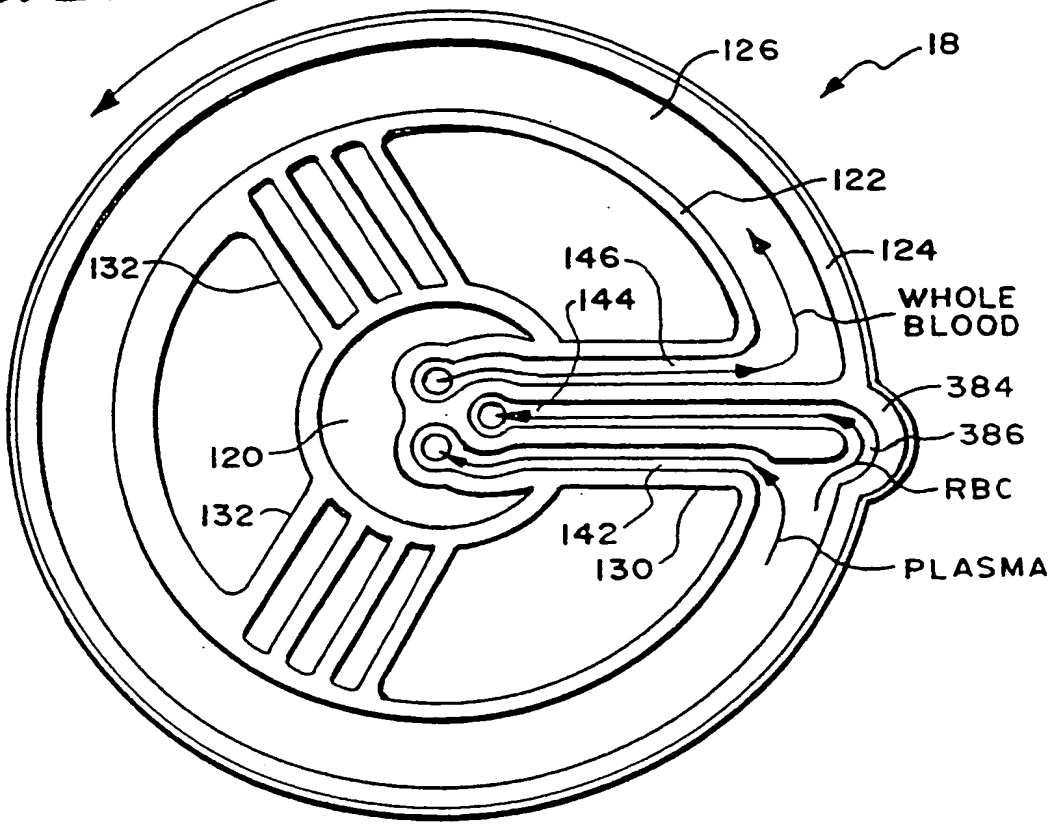

R
126
18
122
124
132
146
144
WHOLE
BLOOD
384
386
120
132
RBC
142
130
PLASMA

FIG 30

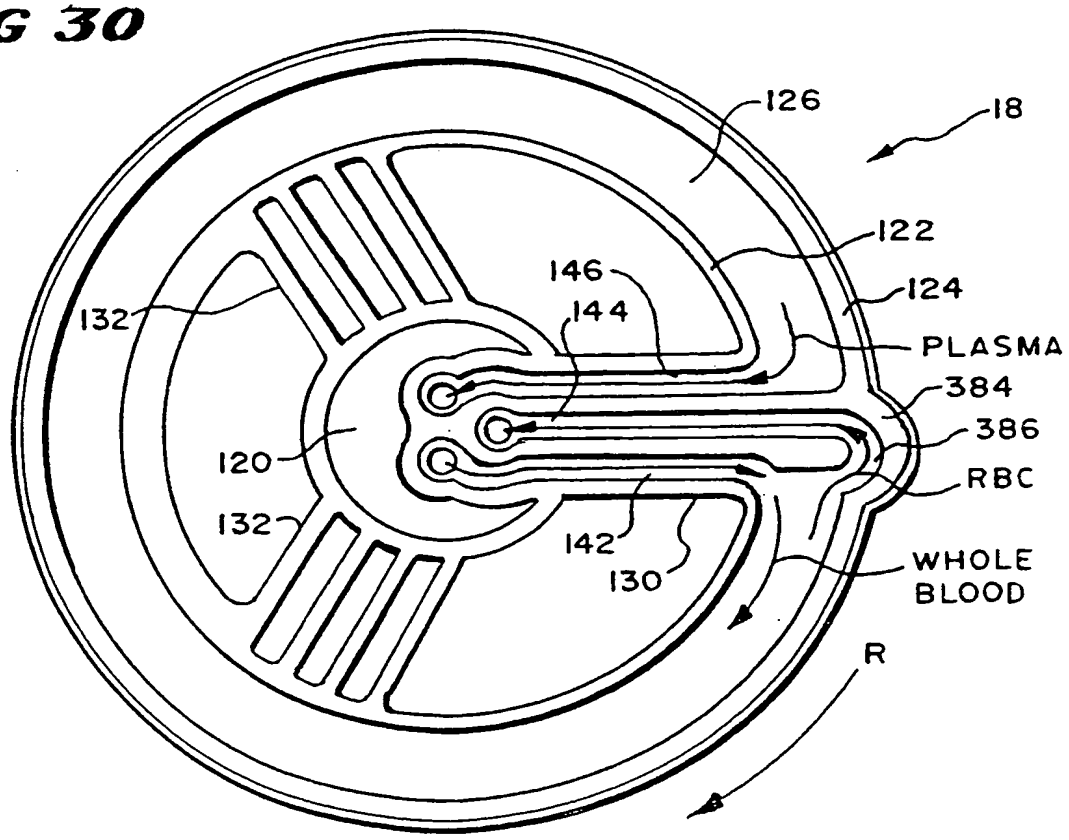
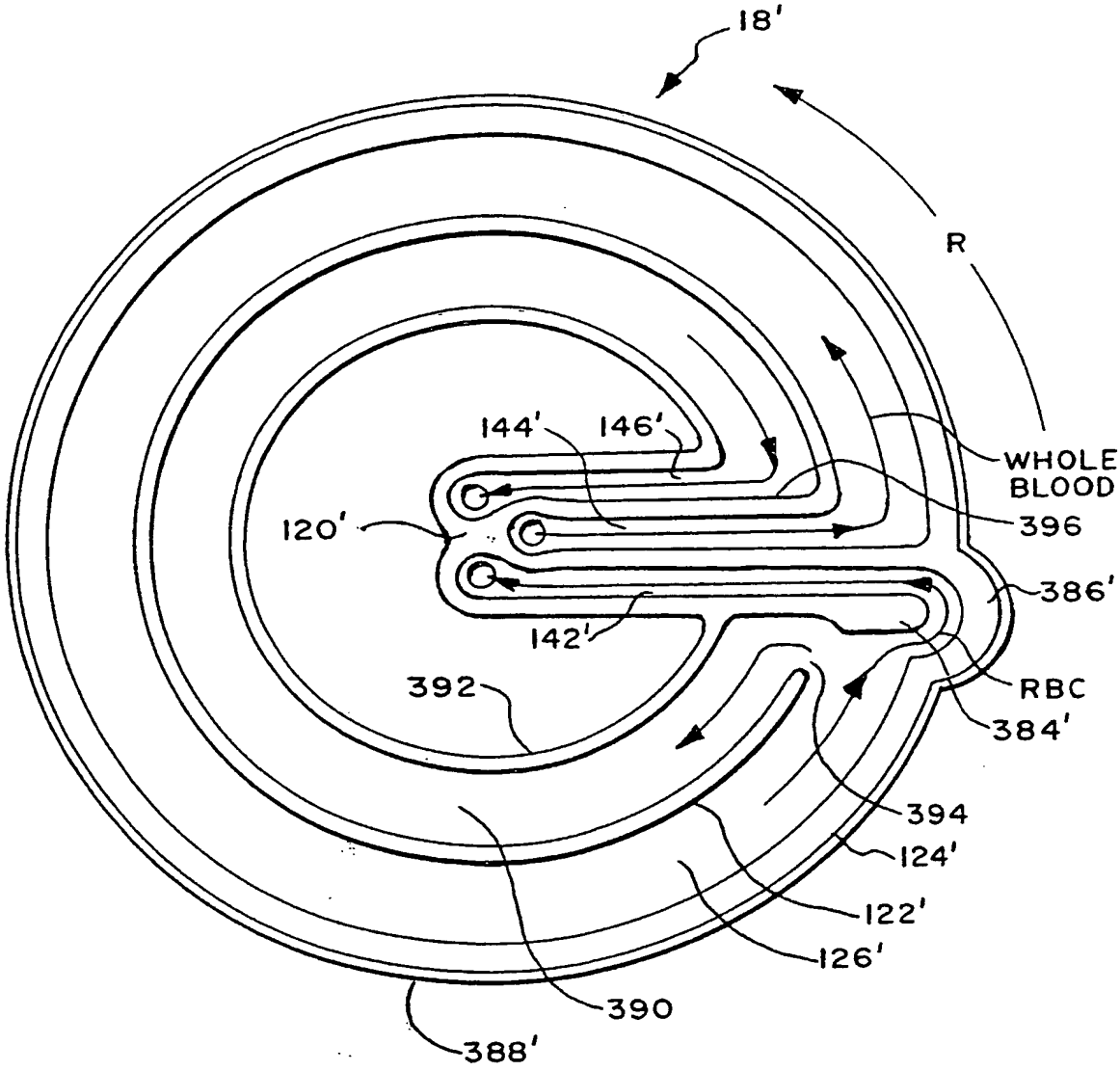

126
18
122
146
124
132
144
PLASMA
384
386
120
RBC
132
142
130
WHOLE
BLOOD
R

FIG 33


18'
R
144'
146'
WHOLE BLOOD
120'
396
386'
142'
392
RBC
384'
394
124'
122'
126'
390
388'

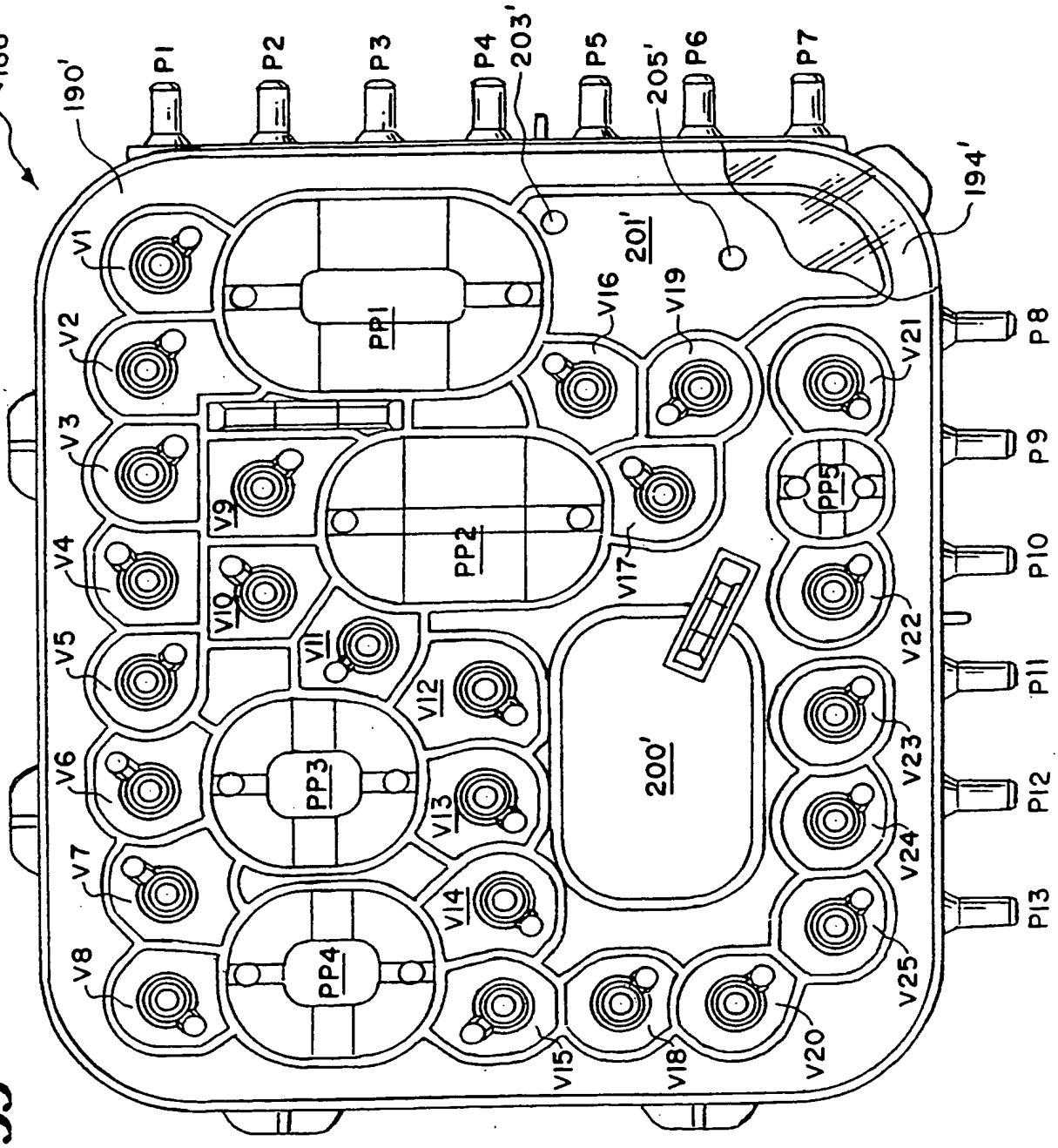


FIG. 35

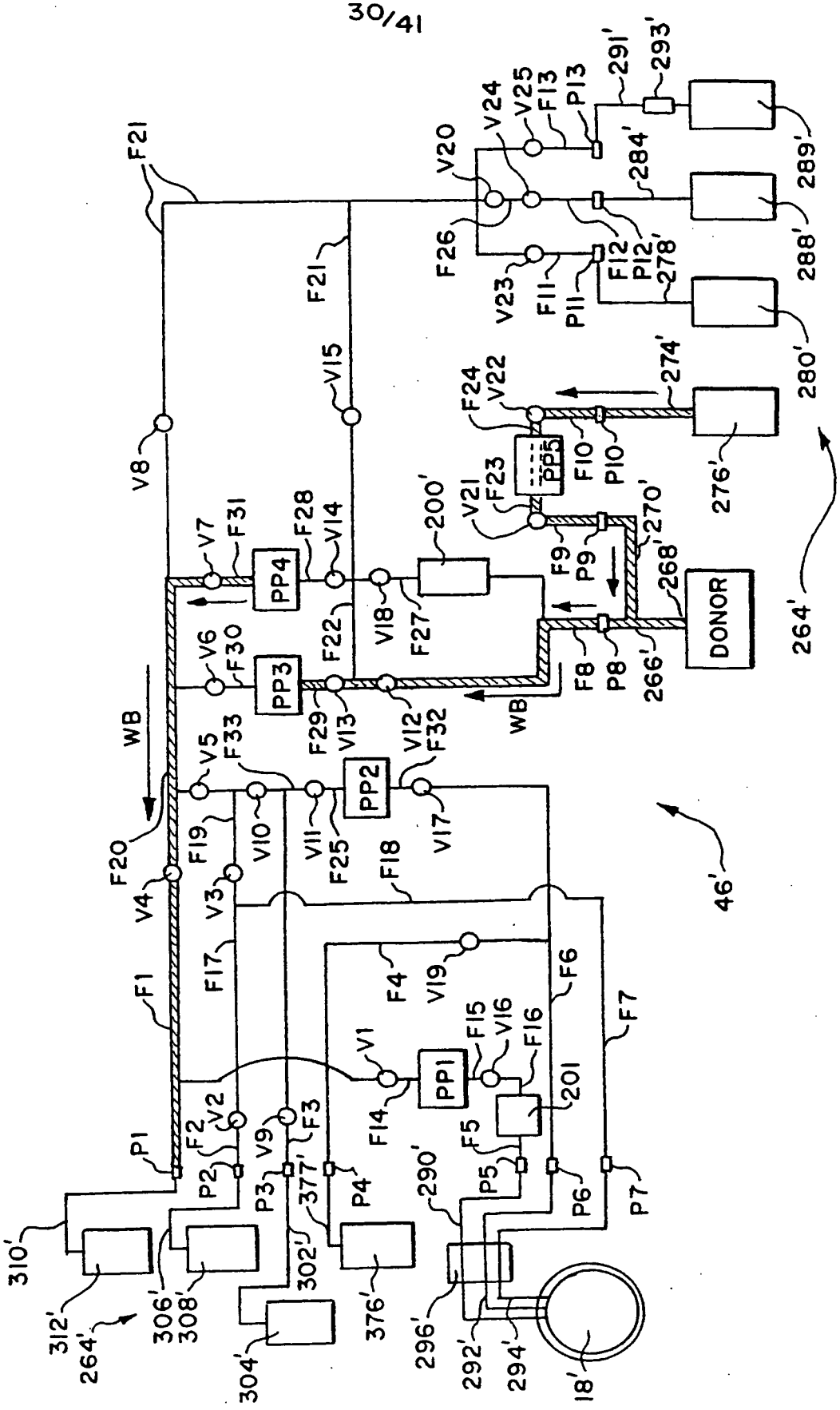

F21
V20
V24
V25
F13
P13
291'
293'
284'
289'
F26
V23
F11
P11
F12
P12
278'
288'
280'
274'
F24
V22
F10
P10
276'
V8
V15
F21
V21
F23
PP5
200'
270'
F9
P9
268'
DONOR
264'
V7
F31
F28
V14
PP4
V18
F27
V6
F30
F22
PP3
F8
P8
266'
WB
V5
F33
F29
V13
V12
F32
PP2
V17
46'
F20
V4
F19
V10
V11
F25
F18
V3
F17
F4
V19
F6
F7
F1
V1
F15
V16
F16
PP1
201
V2
F2
F14
F5
P1
P2
V9
F3
P3
377'
P4
290'
P5
P6
P7
310'
312'
264'
306'
308'
302'
376'
296'
292'
294'
304'
18'

FIG. 37A

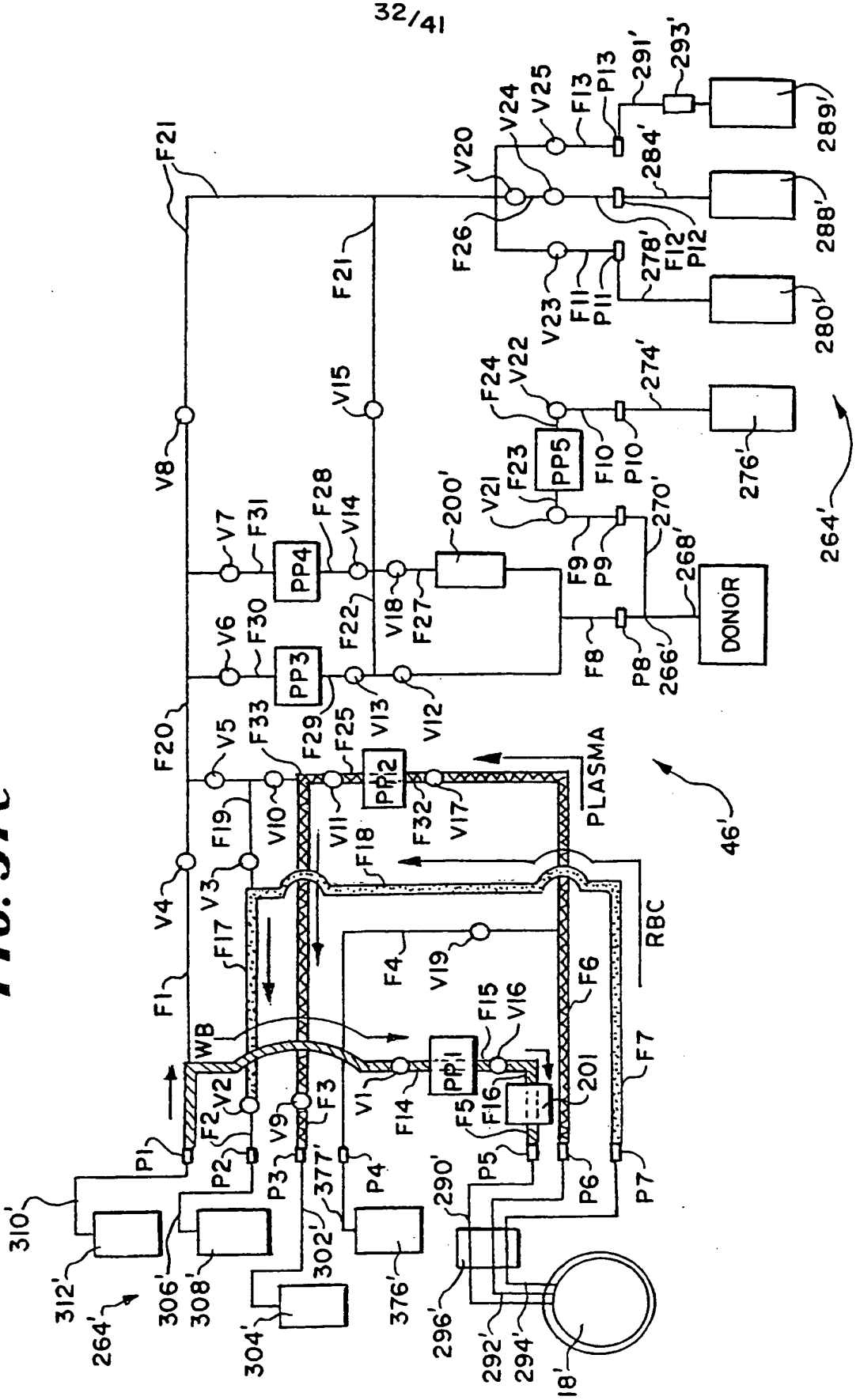


FIG. 37C

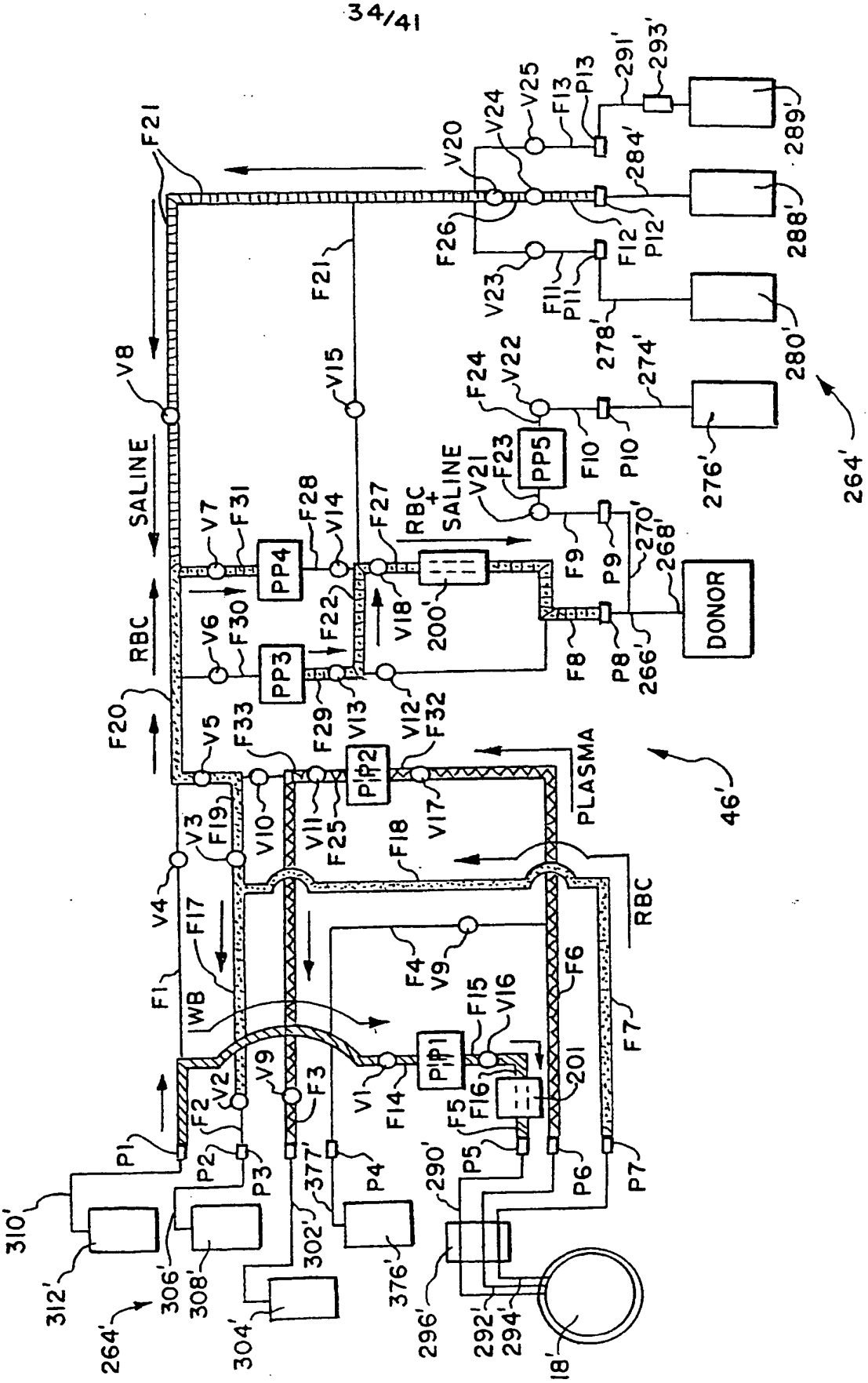


FIG. 37E

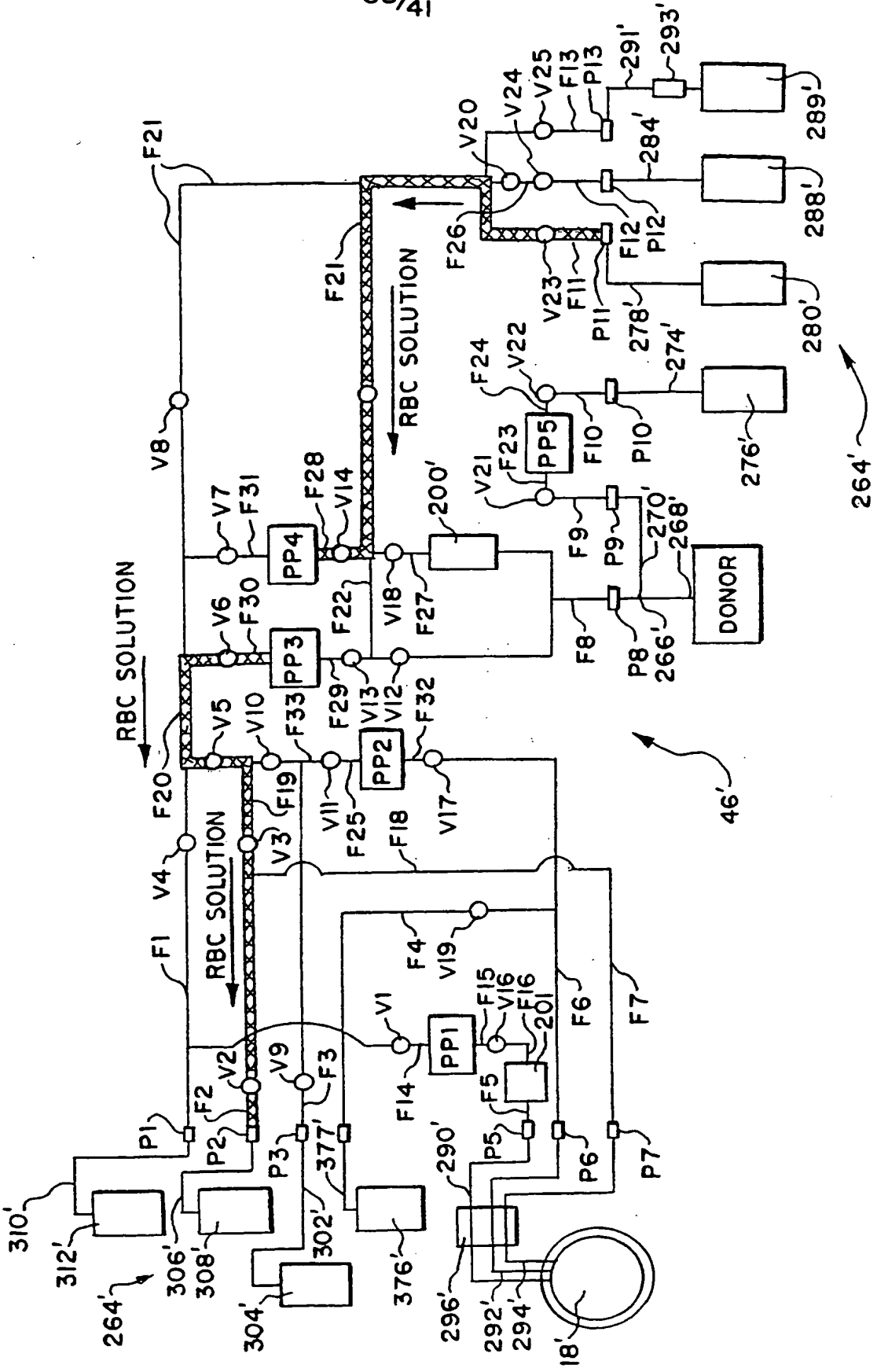


FIG. 38B

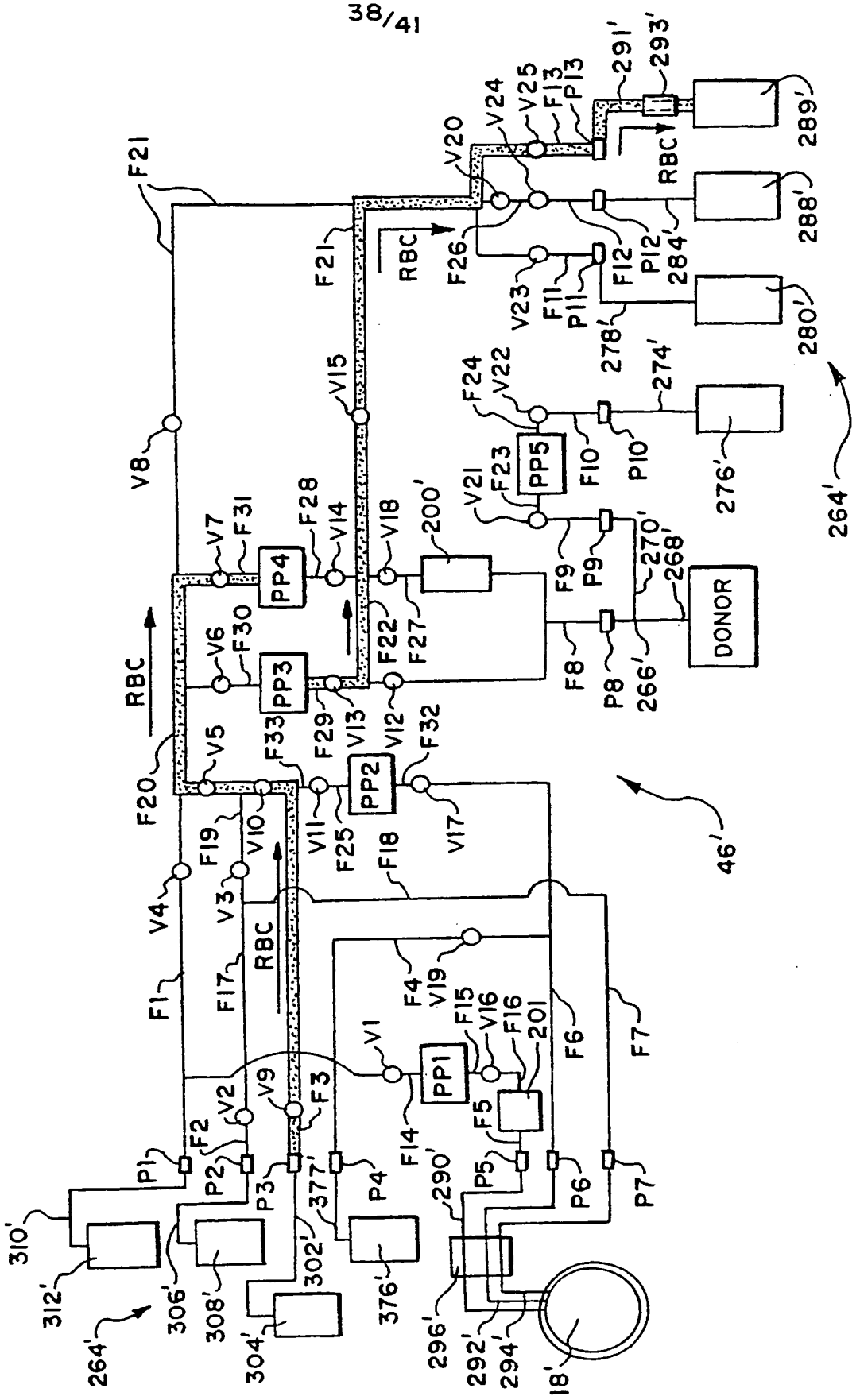
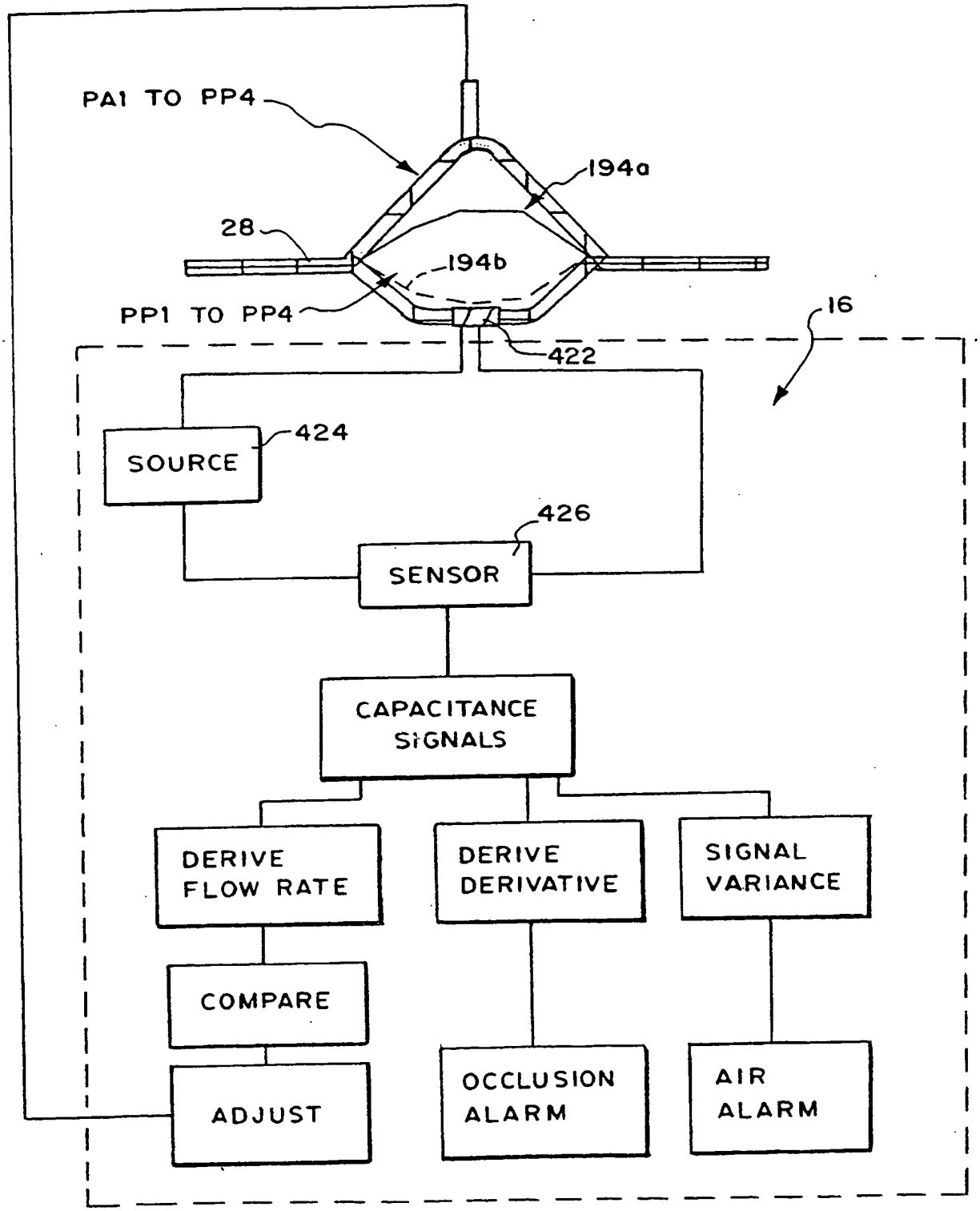


FIG. 39B

FIG. 42


PA1 TO PP4
194a
28
194b
PP1 TO PP4
16
422
SOURCE
424
426
SENSOR
CAPACITANCE SIGNALS
DERIVE FLOW RATE
DERIVE DERIVATIVE
SIGNAL VARIANCE
COMPARE
ADJUST
OCCLUSION ALARM
AIR ALARM

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/23690

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :Please See Extra Sheet.
US CL :604/4.01, 5.01, 6.11; 210/767, 321.67; 417/36, 390
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : Please See Extra Sheet.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EAST
blood, separation, separating, pneumatic, controler, pump(s), valve(s), tubing, cassette, positive, negative, pressure(s)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, Y	US 4,479,761 A (BILSTAD ET AL.) 30 OCTOBER 1984, ENTIRE DOCUMENT.	1, 4, 9-20, 25-29, 32, 37-41, 46 --- 2, 3, 5-8, 21-24, 30, 31, 33-36, 42-45
A	US 4,776,964 A (SCHOENDORFER ET AL.) 11 OCTOBER 1988, FIGS. 2, 4, 8 AND ENTIRE DOCUMENT.	1-46
A	US 5,651,766 A (KINGSLEY ET AL.) 29 JULY 1997, ENTIRE DOCUMENT.	1-46

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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Date of the actual completion of the international search 05 NOVEMBER 2000	Date of mailing of the international search report 01 DEC 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer PATRICIA BIANCO Telephone No. (703) 305-1482

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/23690

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (7):

A61M 37/00; C02F 1/00, 1/44; B01D 37/00, 61/00, 63/00; F04B 49/00, 9/08, 17/00, 35/00

B. FIELDS SEARCHED
Minimum documentation searched
Classification System: U.S.

604/4.01, 5.01, 6.01-05, 6.07, 6.09, 6.1, 6.11, 6.15, 6.16; 210/767, 321.67, 645, 739, 744-45, 780-82, 791, 793, 796-98, 802, 206, 321.6, 321.72; 417/36, 390, 17, 18, 20, 21, 35, 36, 39, 60, 85, 86, 1-4, 375, 384